

FIGURE 1

AGGCGGGCAGCAGCTGCAGGCTGACCTTGCAGCTTGGCGGAATGGACTGGCCTCACAACTGCTGTTTCTT
CTTACCATTTCCATCTTCCTGGGGCTGGGCCAGCCCAGGAGCCCCAAAAGCAAGAGGAAGGGGCAAGGGCG
GCCTGGGCCCCCTGGCCCCCTGGCCCTCACCAGGTGCCACTGGACCTGGTGTACCGATGAAACCGTATGCCC
GCATGGAGGAGTATGAGAGGAACATCGAGGAGATGGTGGCCCAGCTGAGGAACAGCTCAGAGCTGGCCCAG
AGAAAGTGTGAGGTCAACTTGCAGCTGTGGATGTCCAACAAGAGGAGCCTGTCCTCCCTGGGGCTACAGCAT
CAACCACGACCCCAGCCGTATCCCCGTGGACCTGCCGGAGGCACGGTGCCTGTGTCTGGGCTGTGTGAACC
CCTTCACCATGCAGGAGGACCGCAGCATGGTGAGCGTGCCGGTGTTTCAGCCAGGTTCCCTGTGCGCCGCCGC
CTCTGCCCCGCCACCGCCCCGCACAGGGCCTTGCCGCCAGCGCGCAGTCATGGAGACCATCGCTGTGGGCTG
CACCTGCATCTTCTGAATCACCTGGCCCAGAAGCCAGGCCAGCAGCCCCGAGACCATCCTCCTTGACCTTT
GTGCCAAGAAAGGCCTATGAAAAGTAAACACTGACTTTTGAAAGCAAG

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FIGURE 2

MDWPHNLLFLLTISIFLGLGQPRSPKSKRKGQGRPGPLAPGPHQVPLDLVSRMKPYARMEEYERNIEEMVA
QLRNSSELAQRKCEVNLQLWMSNKRSLSPWGYSINHDPRI PVDLPEARCLCLGCVNPFTMQEDRSMVSVF
VFSQVPVRRRLCPPPPRTGPCRQRAVMETIAVGCTCIF

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FIGURE 3

GCCAGGTGTGCAGGCCGCTCCAAGCCCAGCCTGCCCCGCTGCCGCCACCATGACGCTCCTCCCCGGCCTCC
TGTTTCTGACCTGGCTGCACACATGCCTGGCCCACCATGACCCCTCCCTCAGGGGGCACCCCCACAGTCAC
GGTACCCCACTGCTACTCGGCTGAGGAACTGCCCCCTCGGCCAGGCCCCCCCCACACCTGCTGGCTCGAGG
TGCCAAGTGGGGGCAGGCTTTGCCTGTAGCCCTGGTGTCCAGCCTGGAGGCAGCAAGCCACAGGGGGAGGC
ACGAGAGGCCCTCAGCTACGACCCAGTGCCCGGTGCTGCGGCCGGAGGAGGTGTTGGAGGCAGACACCCAC
CAGCGCTCCATCTCACCCCTGGAGATACCGTGTGGACACGGATGAGGACCGCTATCCACAGAAGCTGGCCTT
CGCCGAGTGCCTGTGCAGAGGCTGTATCGATGCACGGACGGGCCGCGAGACAGCTGCGCTCAACTCCGTGC
GGCTGCTCCAGAGCCTGCTGGTGTGCGCCGCCGGCCCTGCTCCCGCGACGGCTCGGGGCTCCCCACACCT
GGGGCCTTTGCCTTCCACACCGAGTTCATCCACGTCCCCGTCGGCTGCACCTGCGTGCTGCCCCGTTTCACT
GTGACCGCCGAGGCCGTGGGGCCCCCTAGACTGGACACGTGTGCTCCCCAGAGGGCACCCCCTATTTATGTG
TATTTATTGTTATTTATATGCCTCCCCCAACTACCCCTGGGGTCTGGGCATTCCCCGTGTCTGGAGGAC
AGCCCCCACTGTTCTCCTCATCTCCAGCCTCAGTAGTTGGGGGTAGAAGGAGCTCAGCACCTCTTCCAGC
CCTTAAAGCTGCAGAAAAGGTGTACACGGCTGCCTGTACCTTGGCTCCCTGTCCTGCTCCCGGCTTCCCT
TACCCTATCACTGGCCTCAGGCCCCGCAGGCTGCCTCTTCCCAACCTCCTTGGAAGTACCCCTGTTTCTTA
ACAATTATTTAAGTGTACGTGTATTATTAACTGATGAACACATCCCCAAAA

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FIGURE 5

GGCTTGCTGAAAATAAAATCAGGACTCCTAACCTGCTCCAGTCAGCCTGCTTCCACGAGGCCTGTCAGTCA
GTGCCCAGACTTGTGACTGAGTGTGCAGTGCCCAGCATGTACCAGGTCAGTGCAGAGGGCTGCCTGAGGGCT
GTGCTGAGAGGGAGAGGAGCAGAGATGCTGCTGAGGGTGGAGGGAGGCCAAGCTGCCAGGTTTGGGGCTGG
GGGCCAAGTGGAGTGAGAACTGGGATCCCAGGGGGAGGGTGCAGATGAGGGAGCGACCCAGATTAGGTGA
GGACAGTTCTCTCATTAGCCTTTTCCCTACAGGTGGTTGCATTCTTGGAATGGTCATGGGAACCCACACCT
ACAGCCACTGGCCCAGCTGCTGCCCCAGCAAAGGGCAGGACACCTCTGAGGAGCTGCTGAGGTGGAGCACT
GTGCCTGTGCCTCCCCTAGAGCCTGCTAGGCCCAACCGCCACCCAGAGTCCTGTAGGGCCAGTGAAGATGGA
CCCCTCAACAGCAGGGCCATCTCCCCCTGGAGATATGAGTTGGACAGAGACTTGAACCGGCTCCCCCAGGA
CCTGTACCACGCCCCGTTGCCTGTGCCCCGCACTGCGTCAGCCTACAGACAGGCTCCCACATGGACCCCCGGG
GCAACTCGGAGCTGCTCTACCACAACCAGACTGTCTTCTACAGGCGGCCATGCCATGGCGAGAAGGGCACC
CACAAGGGCTACTGCCTGGAGCGCAGGCTGTACCGTGTTTCCCTTAGCTTGTGTGTGTGCGGCCCCGTGT
GATGGGCTAGCCGGACCTGCTGGAGGCTGGTCCCTTTTTGGGAAACCTGGAGCCAGGTGTACAACCACTTG
CCATGAAGGGCCAGGATGCCCAGATGCTTGGCCCCTGTGAAGTGCTGTCTGGAGCAGCAGGATCCCGGGAC
AGGATGGGGGGCTTTGGGGAAAACCTGCACTTCTGCACATTTTGAAAAGAGCAGCTGCTGCTTAGGGCCGC
CGGAAGCTGGTGTCTGTCATTTTCTCTCAGGAAAGGTTTTCAAAGTTCTGCCCATTCTGGAGGCCACCA
CTCCTGTCTCTTCCCTCTTTTCCCATCCCCTGCTACCCTGGCCCAGCACAGGCACTTTCTAGATATTTCCCC
CTTGCTGGAGAAGAAAGAGCCCCTGGTTTTATTTGTTTGTACTCATCACTCAGTGAGCATCTACTTTGG
GTGCATTCTAGTGTAGTTACTAGTCTTTTGACATGGATGATTCTGAGGAGGAAGCTGTTATTGAATGTATA
GAGATTTATCCAAATAAATATCTTTATTTAAAAATGAAAAA

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FIGURE 9

CAACTGCACCTCGGTTCTATCGATAGCCACCAGCGCAACATGACAGTGAAGACCCTGCATGGCCCAGCCAT
GGTCAAGTACTTGCTGCTGTGATATTGGGGCTTGCCCTTTCTGAGTGAGGCGGCAGCTCGGAAAATCCCCA
AAGTAGGACATACTTTTTTCCAAAAGCCTGAGAGTTGCCCGCCTGTGCCAGGAGGTAGTATGAAGCTTGAC
ATTGGCATCATCAATGAAAACCAGCGCGTTTCCATGTCACGTAACATCGAGAGCCGCTCCACCTCCCCCTG
GAATTACACTGTCACCTGGGACCCCAACCGGTACCCCTCGGAAGTTGTACAGGCCCAGTGTAGGAACTTGG
GCTGCATCAATGCTCAAGGAAAGGACATCTCCATGAATTCCGTTCCCATCCAGCAAGAGACCCTGGTCGTC
CGGAGGAAGCACCAAGGCTGCTCTGTTTCTTTCCAGTTGGAGAAGGTGCTGGTGACTGTTGGCTGCACCTG
CGTCACCCCTGTCATCCACCATGTGCAGTAAGAGGTGCATATCCACTCAGCTGAAGAAG

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FIGURE 10

MTVKTLHGPMVKYLLLSILGLAFLSEAAARKIPKVGHTFFQKPESCPPVPGGSMKLDIGIINENQRVSMS
RNIESRSTSPWNYTVTWDPNRYPSEVVQAQCRNLGCINAQGKEDISMNSVPIQQETLVVRRKHQGCSVSFQ
LEKVLVTVGCTCVTPVIHHVQ

Signal sequence:

Amino acids 1-30

N-glycosylation site:

Amino acids 83-86

N-myristoylation sites:

Amino acids 106-111;136-141

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FIGURE 11

CCGGCGATGTCGCTCGTGCTGCTAAGCCTGGCCGCGCTGTGCAGGAGCGCCGTACCCCGAGAGCCGACCGT
TCAATGTGGCTCTGAAACTGGGCCATCTCCAGAGTGGATGCTACAACATGATCTAATCCCGGAGACTTGA
GGGACCTCCGAGTAGAACCTGTTACAACAGTGTGCAACAGGGGACTATTCAATTTTGATGAATGTAAGC
TGGGTACTCCGGGCAGATGCCAGCATCCGCTTGTTGAAGGCCACCAAGATTTGTGTGACGGGCAAAAGCAA
CTTCCAGTCCTACAGCTGTGTGAGGTGCAATTACACAGAGGCCTTCCAGACTCAGACCAGACCCCTCTGGTG
GTAAATGGACATTTTCTACATCGGCTTCCCTGTAGAGCTGAACACAGTCTATTTTATTGGGGCCCATAAT
ATTCTAATGCAAATATGAATGAAGATGGCCCTTCCATGTCTGTGAATTTACCTCACCAGGCTGCCTAGA
CCACATAATGAAATATAAAAAAAGTGTGTCAAGGCCGGAAGCCTGTGGGATCCGAACATCACTGCTTGTA
AGAAGAATGAGGAGACAGTAGAAGTGAAGTTCACAACCACTCCCTGGGAAACAGATACATGGCTCTTATC
CAACACAGCACTATCATCGGGTTTTCTCAGGTGTTTGAGCCACACCAGAAGAAACAAACGCGAGCTTCAGT
GGTGATTCCAGTGACTGGGGATAGTGAAGGTGCTACGGTGCAGCTGACTCCATATTTTCTACTTGTGGCA
GCGACTGCATCCGACATAAAGGAACAGTTGTGCTCTGCCCACAAACAGGCGTCCCTTTCCCTCTGGATAAC
AACAAAAGCAAGCCGGGAGGCTGGCTGCCTCTCCTCCTGCTGTCTCTGCTGGTGGCCACATGGGTGCTGGT
GGCAGGGATCTATCTAATGTGGAGGCACGAAAGGATCAAGAAGACTTCCTTTTCTACCACCACACTACTGC
CCCCATTAAGGTTCTTGTGGTTTACCCATCTGAAATATGTTTCCATCACACAATTTGTTACTTCACTGAA
TTTCTTCAAAACCATTGCAGAAGTGAAGTTCATCCTTGAAAAGTGGCAGAAAAAGAAAATAGCAGAGATGGG
TCCAGTGCAAGTGGCTTGCCACTCAAAGAAGGCAGCAGACAAAGTCGTCTTCTTCTTCCAATGACGTCA
ACAGTGTGTGCGATGGTACCTGTGGCAAGAGCGAGGGCAGTCCAGTGAGAACTCTCAAGACCTCTTCCCC
CTTGCCTTTAACCTTTTCTGCAGTGATCTAAGAAGCCAGATTCTATCTGCACAAATACGTGGTGGTCTACTT
TAGAGAGATTGATACAAAAGACGATTACAATGCTCTCAGTGTCTGCCCCAAGTACCACCTCATGAAGGATG
CCACTGCTTTCTGTGCAGAACTTCTCCATGTCAAGCAGCAGGTGTCAGCAGGAAAAAGATCACAAGCCTGC
CACGATGGCTGCTGCTCCTTGTAAG

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FIGURE 12

MSLVLLSLAALCRSAVPREPTVQCGSETGPSPEWMLQHDLI PGDLRLDLRVEPVTTTSVATGDYSILMNVSWV
 LRADASIRLLKATKICVTGKSNFQSYSCVRCNYTEAFQTQTRPSGGKWTF SYIGFPVELNTVYFIGAHNIP
 NANMNEDGPSMSVNFTSPGCLDHIMKYKKKCVKAGSLWDPNITACKKNEETVEVNFTTTPLGNRYMALIQH
 STIIGFSQVFEPHQKKQTRASVVI PVTGDSEGATVQLTPYFPTCGSDCIRHKGTVVLC PQTGVFPFLDNNK
 SKPGGWLPLLLLSLLVATWVLVAGIYLMWRHERIKKTSFSTTTLLPPIKVLVVYPSEICFHHTICYFTEFL
 QNHCRSEVILEKWQKKKIAEMGPVQWLATQKKAADKVVFLLSNDVNSVCDGTCGKSEGSPSENSQDLFPLA
 FNLFCSDLRSQIHLHKYVVVYFREIDTKDDYNALSVC PKYHLMKDATAFCAELLHV KQQVSAGKRSQACHD
 GCCSL

Signal sequence:	Amino acids 1-14
Transmembrane domain:	Amino acids 290-309
N-glycosylation sites:	Amino acids 67-70;103-106;156-159; 183-186;197-200;283-286
cAMP- and cGMP-dependent protein kinase phosphorylation sites:	Amino acids 228-231;319-322
N-myristoylation site:	Amino acids 116-121
Amidation site:	Amino acids 488-491

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FIGURE 13

ACACTGGCCAAACAAAAACGAAAGCACTCCGTGCTGGAAGTAGGAGGAGAGTCAGGACTCCCAGGACAGAG
AGTGCAAAACTACCCAGCACAGCCCCCTCCGCCCCCTCTGGAGGCTGAAGAGGGATTCCAGCCCCCTGCCA
CCCACAGACACGGGCTGACTGGGGTGTCTGCCCCCTTGGGGGGGGCAGCACAGGGCCTCAGGCCTGGGT
GCCACCTGGCACCTAGAAGATGCTGTGCCCTGGTTCTTGCTGTCTTGGCACTGGGGCCGAAGCCCAGTGG
TCCTTTCTCTGGAGAGGCTTGTGGGGCCTCAGGACGCTACCCACTGCTCTCCGGGCCTCTCTGCCGCCTC
TGGGACAGTGACATACTCTGCCTGCCTGGGGACATCGTGCCTGCTCCGGGCCCCGCTGCTGGCGCCTACGCA
CCTGCAGACAGAGCTGGTGCTGAGGTGCCAGAAGGAGACCGACTGTGACCTCTGTCTGCGTGTGGCTGTCC
ACTTGGCCGTGCATGGGCACTGGGAAGAGCCTGAAGATGAGGAAAAGTTTGGAGGAGCAGCTGACTCAGGG
GTGGAGGAGCCTAGGAATGCCTCTCTCCAGGCCCAAGTCGTGCTCTCCTTCCAGGCCTACCCTACTGCCCC
CTGCGTCTGCTGGAGGTGCAAGTGCCTGCTGCCCTTGTGCAGTTTGGTCAGTCTGTGGGCTCTGTGGTATAT
GACTGCTTCGAGGCTGCCCTAGGGAGTGAGGTACGAATCTGGTCCATACTCAGCCCAGGTACGAGAAGGA
ACTCAACCACACACAGCAGCTGCCTGCCCTGCCCTGGCTCAACGTGTCAGCAGATGGTGACAACGTGCATC
TGGTTCTGAATGTCTCTGAGGAGCAGCACTTCGGCCTCTCCCTGTACTGGAATCAGGTCCAGGGCCCCCA
AAACCCCGGTGGCACAAAACCTGACTGGACCGCAGATCATTACCTTGAACCACACAGACCTGGTTCCCTG
CCTCTGTATTACAGGTGTGGCCTCTGGAACCTGACTCCGTTAGGACGAACATCTGCCCCCTCAGGGAGGACC
CCCGCGCACACCAGAACCTCTGGCAAGCCGCCGACTGCGACTGCTGACCTGCAGAGCTGGCTGCTGGAC
GCACCGTGCTCGCTGCCCCGAGAAGCGGCACTGTGCTGGCGGGCTCCGGGTGGGGACCCCTGCCAGCCACT
GGTCCCACCGCTTTCCTGGGAGAACGTCACTGTGGACAAGGTTCTCGAGTTCCCATTGCTGAAAGGCCACC
CTAACCTCTGTGTTACAGGTGAACAGCTCGGAGAAGCTGCAGCTGCAGGAGTGCTTGTGGGCTGACTCCCTG
GGGCCTCTCAAAGACGATGTGCTACTGTTGGAGACACGAGGCCCCCAGGACAACAGATCCCTCTGTGCCTT
GGAACCCAGTGGCTGTACTTCACTACCCAGCAAAAGCCTCCACGAGGGCAGCTCGCCTTGGAGAGTACTTAC
TACAAGACCTGCAGTCAGGCCAGTGTCTGCAGCTATGGGACGATGACTTGGGAGCGCTATGGGCCTGCCCC
ATGGACAAATACATCCACAAGCGCTGGGCCCTCGTGTGGCTGGCCTGCCTACTCTTTGCCGCTGCGCTTTC
CCTCATCCTCCTTCTCAAAAAGGATCACGCGAAAGGGTGGCTGAGGCTCTTGAAACAGGACGTCCGCTCGG
GGGCGGCCCGCAGGGGGCCGCGGGCTCTGCTCCTCTACTCAGCCGATGACTCGGGTTTCGAGCGCCTGGTG
GGCGCCCTGGCGTCGGCCCTGTGCCAGCTGCCGCTGCGCGTGGCCGTAGACCTGTGGAGCCGTCTGAACT
GAGCGCGCAGGGGGCCGCTGGTTTACGCGCAGCGCGCCAGACCCTGCAGGAGGGCGGCGTGGTG
TCTTGCTCTTCTCTCCCGGTGCGGTGGCGCTGTGCAGCGAGTGGCTACAGGATGGGGTGTCCGGGCCCCGG
GCGCACGGCCCGCACGACGCTTCCGCGCCTCGCTCAGCTGCGTGCTGCCCCACTTCTTGAGGGCCGGGC
GCCCCGACGCTACGTGGGGGCTGCTTCGACAGGCTGCTCCACCCGGACGCCGTACCCGCCCTTTTCCGCA
CCGTGCCCGTCTTCACTGCCCCTCCAACTGCCAGACTTCTTGGGGGCCCTGCAGCAGCCTCGCGCCCCG
CGTTCGGGGCGGCTCCAAGAGAGAGCGGAGCAAGTGTCCCGGGCCCTTCAGCCAGCCCTGGATAGCTACTT
CCATCCCCCGGGGACTCCCGCGCCGGGACGCGGGGTGGGACCAGGGGCGGGACCTGGGGCGGGGGACGGGA
CTTAAATAAAGGCAGACGCTGTTTTTCTAAAAAA

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FIGURE 14

MPVPWFLLSLALGRSPVVLSELERLVGPQDATHCSPGLSCRLWDSILCLPGDIVPAPGPVLAPTHLQTELV
 LRCQKETDCDLCLRVAVHLAVHGHWEPEDEEKFGGAADSGVEEPRNASLQAQVVLSFQAYPTARCVLLEV
 QVPAALVQFGQSVGSSVYDCFEAALGSEVRIWSYTQPRYEKELNHTQQLPALPWLNVNSADGDNVHLVLNV
 EEQHFGLSLYWNQVQGPPKPRWHKNLTGPGIITLNHTDLVPCLCIQVWPLEPDSVRTNICPFREDPRAHQ
 LWQAARLRLTLQSWLLDAPCSLPAEAALCWRAPGGDPCQPLVPPLSWENVTVDKVLEFPLLKGHPNLCVQ
 VNSSEKLQLQECLWADSLGPLKDDVLLLETRGPQDNRSLEPSGCTSLPSKASTRAARLGEYLLQDLQS
 GQCLQLWDDDLGALWACPMCKYIHKRWALVWLACLLFAAALSLLLLKKDHAKGWLRLKQDVRSGAAARG
 RAALLLYSADDSGFERLVGALASALCQLPLRVAVDLWSRRELSAQGPVAVFHAQRRQTLQEGGVVLLFSP
 GAVALCSEWLQDGVSGPGAHGPHDAFRASLSCVLPDFLQGRAPGSYVGACFDRLHPDAVPALFRTVPVFT
 LPSQLPDFLGALQQPRAPRSGRLLQERAEQVSRAALQPALDSYFHPPGTPAPGRGVGPGAGPGAGDGT

signal sequence:	Amino acids 1-20
transmembrane domain:	Amino acids 453-473
N-glycosylation sites:	Amino acids 118-121;186-189;198-201; 211-214;238-241;248-251;334-337; 357-360;391-394
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Glycosaminoglycan attachment site:	Amino acids 583-586
cAMP- and cGMP-dependent protein kinase phosphorylation site:	Amino acids 552-555
N-myristoylation sites:	Amino acids 107-112;152-157;319-324; 438-443;516-521;612-617;692-697; 696-701;700-705

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FIGURE 16

MGSSRLAALLPLLLIVIDLSDSAGIGFRHLPHWNTRCPLASHTDDSFSGSSAYIPCRTWWALFSTKPWCV
RVWHCSRCLCQHLLSGGSLQRGLFHLLVQSKKSSTFKFYRRHKMPAPAQRKLLPRRHLSEKSHHISIPS
PDISHKGLRSKRTQPSDPETWESLPRLDSQRHGGPEFSFDLLPEARAIRVTISSGPEVSVRLCHQWALECE
ELSSPYDVQKIVSGGHTVELPYEFLLPCLCIEASYLQEDTVRRKKCPFQSWPEAYGSDFWKSVHFTDYSQH
TQMVMALTLCPLKLEAALCQRHDWHTLCKDLPNATARESDGWYVLEKVDLHPQLCFKFSFGNSSHVECPH
QTGSLTSWNVSMDTQAQQLILHFSSRMHATFSAAWSLPGLGQDTLVPPVYTVSQARGSSPVSLDLIIPFLR
PGCCVLVWRSDVQFAWKHLLCPDVSYRHLGLLILALLALLTLLGVVLALTLCRRPQSGPGPARPVLLLHAAD
SEAQRRLVGALAELLRAALGGGRDVIVDLWEGRHVARVGPLPWLWAARTRVAREQGTVLLLWSGADLRPVS
GPDPRAPLLALLHAAPRPLLLLAYFSRLCAKGDIPPLRALPRYRLRLDLPRLLRALDARPF AEATSWGR
LGARQRRQRSRLELC SRLERE AARLADLG

Signal peptide:	Amino acids 1-23
Transmembrane domain:	Amino acids 455-472
N-glycosylation sites:	Amino acids 318-322;347-351;364-368
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Glycosaminoglycan attachment site:	Amino acids 482-486
cAMP- and cGMP-dependent protein kinase phosphorylation sites:	Amino acids 104-108;645-649
Tyrosine kinase phosphorylation site:	Amino acids 322-329
N-myristoylation sites:	Amino acids 90-96;358-364;470-476
Eukaryotic cobalamin-binding proteins:	Amino acids 453-462

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FIGURE 17

GCCAGGCCCTATCTCCCTGCCAGGAGGCCGGAGTGGGGGAGGTGAGACGGGGCGGTTGGAGGGGGAGGGAT
GCCACGCGCTTCTGCCTCAGGTGTTCTGCGTTGTTTGTGTCAGTGGAGAGCAGGGAGTGGGGCCAGCCAGCA
GAAACAGTGGGCTGTACAACATCACCTTCAAATATGACAATTGTACCACCTACTTGAATCCAGTGGGGAAG
CATGTGATTGCTGACGCCCAGAATATCACCATCAGCCAGTATGCTTGCCATGACCAAGTGGCAGTCACCAT
TCTTTGGTCCCCAGGGGCCCTCGGCATCGAATTCCTGAAAGGATTTTCGGGTAATACTGGAGGAGCTGAAGT
CGGAGGGAAGACAGTGCCAAACACTGATTCTAAAGGATCCGAAGCAGCTCAACAGTAGCTTCAAAGAAGT
GGAATGGAATCTCAACCTTTCTGAATATGAAATTTGAAACGGATTATTTTCGTAAAGGTTGTCCCTTTTCC
TTCCATTAAAAACGAAAGCAATTACCACCCTTTCTTCTTTAGAACCCGAGCCTGTGACCTGTTGTTACAGC
CGGACAATCTAGCTTGTAACCCCTTCTGGAAGCCTCGGAACCTGAACATCAGCCAGCATGGCTCGGACATGC
AGGTGTCCTTCGACCACGCACCCGCATGGCTCGGACATGCAGGTGTCCTTCGACCACGCACCCGCACAACTTC
GGCTTCCGTTTCTTCTATCTTCACTACAAGCTCAAGCACGAAGGACCTTTCAAGCGAAAGACCTGTAAGCA
GGAGCAAACACAGAGATGACCAGCTGCCTCCTTCAAATGTTTCTCCAGGGGATTATATAATTGAGCTGG
TGGATGACACTAACACAACAAGAAAAGTGATGCATTATGCCTTAAAGCCAGTGCCTCCCCGTGGGCCGGG
CCCATCAGAGCCGTGGCCATCACAGTGCCACTGGTAGTCATATCGGCATTCGCGACGCTCTTCACTGTGAT
GTGCCGCAAGAAGCAACAAGAAAATATATATTACATTTAGATGAAGAGAGCTCTGAGTCTTCCACATACA
CTGCAGCACTCCCAAGAGAGAGGCTCCGGCCGCGGCCGAAGGTCTTTCTCTGCTATTCCAGTAAAGATGGC
CAGAATCACATGAATGTGTCCTCAGTGTTTCGCCTACTTCCTCCAGGACTTCTGTGGCTGTGAGGTGGCTCT
GGACCTGTGGGAAGACTTCAGCCTCTGTAGAGAAGGGCAGAGAGAATGGGTCAATCCAGAAGATCCACGAGT
CCCAGTTCATCATTGTGGTTTGTTCCAAAGGTATGAAGTACTTTGTGGACAAGAAGAACTACAAACACAAA
GGAGGTGGCCGAGGCTCGGGGAAAGGAGAGCTCTTCTGTTGGCGGTGTCAGCCATTGCCGAAAAGCTCCG
CCAGGCCAAGCAGAGTTTCGTCCGCGGCGCTCAGCAAGTTTATCGCCGTCTACTTTGATTATTCTGCGAGG
GAGACGTCCCCGGTATCCTAGACCTGAGTACCAAGTACAGACTCATGGACAATCTTCTCAGCTCTGTTCC
CACCTGCACTCCCGAGACCACGGCCTCCAGGAGCCGGGGCAGCACACGCGACAGGGCAGCAGAAGGAACTA
CTTCCGGAGCAAGTCAGGCCGGTCCCTATACGTCGCCATTTGCAACATGCACCAGTTTATTGACGAGGAGC
CCGACTGGTTTCGAAAAGCAGTTTCGTTCCCTTCCATCCTCCTCCACTGCGCTACCGGGAGCCAGTCTTGAG
AAATTTGATTTCGGGCTTGGTTTTAAATGATGTCATGTGCAAACCAGGGCCTGAGAGTGAATCTGCTTAA
GGTAGAGGCGGCTGTTCTTGGGGCAACCGGACCAGCCGACTCCCAGCACGAGAGTCAGCATGGGGGCCTGG
ACCAAGACGGGGAGGCCCGGCCTGCCCTTGACGGTAGCGCCGCCCTGCAACCCCTGCTGCACACGGTGAAA
GCCGGCAGCCCTCGGACATGCCGCGGGACTCAGGCATCTATGACTCGTCTGTGCCCTCATCCGAGCTGTC
TCTGCCACTGATGGAAGGACTCTCGACGGACCAGACAGAAACGTCTTCCCTGACGGAGAGCGTGTCTCTCT
CTTCAGGCCTGGGTGAGGAGGAACCTCCTGCCCTTCTTCCAAGCTCCTCTCTTCTGGGTGATGCAAAGCA
GATCTTGGTTGCCGAGCTACACTGATGAATCCACGCGGTGCCCCCTTTGTAACAAAACGAAAGAGTCTA
AGCATTGCCACTTTAAAAA

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FIGURE 15

CGAGGGCTCCTGCTGGTACTGTGTTGCTGCTGCACAGCAAGGCCCTGCCACCCACCTTCAGGCCATGCAG
CCATGTTCCGGGAGCCCTAATTGCACAGAAGCCC**ATG**GGGAGCTCCAGACTGGCAGCCCTGCTCCTGCCTC
TCCTCCTCATAGTCATCGACCTCTCTGACTCTGCTGGGATTGGCTTTCGCCACCTGCCCCACTGGAACACC
CGCTGTCCTCTGGCCTCCACACGGATGACAGTTTCACTGGAAGTTCTGCCTATATCCCTTGCCGCACCTG
GTGGGCCCTCTTCTCCACAAAGCCTTGGTGTGTGCGAGTCTGGCACTGTTCCCGCTGTTTGTGCCAGCATCTGC
TGTCAGGTGGCTCAGGTCTTCAACGGGGCCTCTTCCACCTCCTGGTGCAGAAATCCAAAAAGTCTTCCACA
TTCAAGTTCTATAGGAGACACAAGATGCCAGCACCTGCTCAGAGGAAGCTGCTGCCTCGTCGTCACCTGTC
TGAGAAGAGCCATCACATTTCCATCCCCTCCCCAGACATCTCCACAAAGGGACTTCGCTCTAAAAGGACCC
AACCTTCGGATCCAGAGACATGGGAAAGTCTTCCCAGATTGGACTCACAAAGGCATGGAGGACCCGAGTTC
TCCTTTGATTTGCTGCCTGAGGCCCGGGCTATTGCGGTGACCATATCTTCAGGCCCTGAGGTCAGCGTGCG
TCTTTGTCACCACTGGGCACTGGAGTGTGAAGAGCTGAGCAGTCCCTATGATGTCCAGAAAATTGTGTCTG
GGGGCCACACTGTAGAGCTGCCTTATGAATTCCTTCTGCCCTGTCTGTGCATAGAGGCATCCTACCTGCAA
GAGGACACTGTGAGGCGCAAAAATGTCCCTTCAGAGCTGGCCAGAAGCCTATGGCTCGGACTTCTGGAA
GTCAGTGCACCTTCACTGACTACAGCCAGCACACTCAGATGGTCATGGCCCTGACACTCCGCTGCCCCACTGA
AGCTGGAAGCTGCCCTCTGCCAGAGGCACGACTGGCATACCCTTTGCAAAGACCTCCCGAATGCCACGGCT
CGAGAGTCAGATGGGTGGTATGTTTTGGAGAAGGTGGACCTGCACCCCCAGCTCTGCTTCAAGTTCTCTTT
TGGAACAGCAGCCATGTTGAATGCCCCCACCAGACTGGGTCTCTCACATCCTGGAATGTAAGCATGGATA
CCCAAGCCCAGCAGCTGATTCTTCACTTCTCCTCAAGAATGCATGCCACCTTCAGTGCTGCCTGGAGCCTC
CCAGGCTTGGGGCAGGACACTTTGGTGCCCCCGTGTACACTGTCAGCCAGGCCCGGGGCTCAAGCCCAGT
GTCACTAGACCTCATCATTCCTTCCCTGAGGCCAGGGTGCTGTGTCTGCTGGTGTGGCGGTGAGATGTCCAGT
TTGCCTGGAAGCACCTCTTGTGTCCAGATGTCTCTTACAGACACCTGGGGCTCTTGATCCTGGCACTGCTG
GCCCTCCTCACCCCTACTGGGTGTTGTTCTGGCCCTCACCTGCCGGCGCCACAGTCAGGCCCGGGCCAGC
GCGGCCAGTGCTCCTCCTGCACGCGCGGACTCGGAGGCGCAGCGCGCCTGGTGGGAGCGCTGGCTGAAC
TGCTACGGGCAGCGCTGGGCGGCGGGCGGACGTGATCGTGACCTGTGGGAGGGGAGGCACGTGGCGCGCGT
'GGGCCCCGCTGCCGTGGCTCTGGGCGGCGGGACGCGCGTAGCGGGAGCAGGGCACTGTGCTGCTGCTGT
GGAGCGGCGCCGACCTTCGCCCCGTGACGCGCCCCGACCCCGCGCCGCGCCCCCTGCTCGCCCTGCTCCAC
GCTGCCCCGCGCCCGCTGCTGCTGCTCGCTTACTTCAGTCGCCTCTGCGCCAAGGGCGACATCCCCCGCC
GCTGCGCGCCCTGCCGCGCTACCGCCTGCTGCGCGACCTGCCGCGTCTGCTGCGGGCGCTGGACGCGCGGC
CTTTCGAGAGGCCACCAGCTGGGGCCGCTTGGGGCGCGGCAGCGCAGGCAGAGCCGCTAGAGCTGTGC
AGCCGGCTTGAACGAGAGGCCGCCGACTTGACAGCTAGGTTGAGCAGAGCTCCACCGCAGTCCCGGGTGTCT

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FIGURE 18

MPRASASGV PALFVS GEQGVGPASRNSGLYNITFKYDNCTTYLNPVGKHVIADAQNITISQYACHDQVAVT
 ILWSPGALGIEFLKGFRVILEELKSEGRQCQQLILKDPKQLNSSFKRTGMESQPFLLNMKFETDYFVKVVPF
 PSIKNESNYHPFFFRTRACDLLLQPDNLACKPFWKPRNLNISQHGSDMQVSFDHAPHGSDMQVSFDHAPHN
 FGFRFFYLHYKLKHEGPFKRKTCKQEQTTEMTSCLLQNVSPGDYIIELVDDTNTTRKVMHYALKPVHSPWA
 GPIRAVAITVPLVVISAFATLFTVMCRKKQQENIYSHLDEESSESSTYTAALPRERLRPRPKVFLCYSSKD
 GQNHMNVVQCFAYFLQDFCGCEVALDLWEDFSLCREGQREWVIQKIHESQFIIIVVCSKGMKYFVDKKNYKH
 KGGGRGSGKGELFLVAVSAIAEKL RQAKQSSSAALS KFI AVYFDYSCEGDVPGILD LSTKYRLMDNLPQLC
 SHLHSRDHGLQEPGQHTRQGSRRNYFRSKSGRS LYVAICNMHQFIDEEDWFEKQFVFPFHPPLRYREPVL
 EKFD SGLVLNDVMCKPGPESDFCLKVEAAVLGATGPADSQHESQHGGLDQDGEARPALDGSAALQPLLHTV
 KAGSPSDMPRDSGIYDSSVPSSLSLPLMEGLSTDQTETSSLTESVSSSSGLGEEEPALPSKLLSSGSK
 ADLGCRSYTDELHAVAPL

Transmembrane domain:

Amino acids 283-307

N-glycosylation sites:

Amino acids 31-34;38-41;56-59;
 113-116;147-150;182-185;266-269

~~Glycosaminoglycan attachment sites: Amino acids 433-436;689-692~~

cAMP- and cGMP-dependent protein kinase phosphorylation:

Amino acids 232-235

Tyrosine kinase phosphorylation sites:

Amino acids 312-319;416-424

N-myristoylation site:

Amino acids 19-24;375-380;428-433;
 429-434;432-437;517-522;574-579;
 652-657;707-712

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FIGURE 19

h-IL17 1 MTPGKTSLVSL L L L S L E A I V K A G I T I P R
h-IL17B 1 MDWPHNLLFLLTISIFLGLGQPRSPKSKRKGOGR P G P L A P G P
h-IL17C 1 M T L L P G L L F L T W L H T C L A H D P S L R G H P H S H G T P H C Y S A E E L P L G Q A P P H
h-IL17D 1 M L V A G F L L A L P P S W A A G A P R A G R R P A R P R G C A D R P
h-IL17E 1 M R E R P R L G E D S S L I S L F L O V V A F L A M V M G T H T Y S H
h-IL17F 1 M T V K T L H G P A M V K Y L L S I L G L A F L S E A A R K I P K V G

h-IL17 30 N P G C P N S E D K N F P R T V M V N L N I H N R N T N T N P K R S S D
h-IL17B 43 H Q V P L D L V S R M K P Y A R M E E Y E R N I E E M V A O L R N S S E L A O R K C E V N L Q L W M
h-IL17C 51 L L A R G A K W G O A L P V A L V S S L E A A S H R G R H E R P S A T T O C P V L R P E E V L E A D
h-IL17D 36 E E L L E Q L Y G R L A A G V L S A F H H T L Q L G P R E Q A R N N A S C P A G G R P A D R R F R P P
h-IL17E 36 W P S C C P S K G O D T S E E L L R W S T V P V P P L E P A R P N R H P E S C R A S E D G P
h-IL17F 38 H T F F Q K P E S C P P V P G G S M K L D I G I I N E N O R V S M S R N

h-IL17 66 Y Y N R S T S P W N L H R N E D P E R Y P S V I W E A K C R H L G C I N A D G N V O Y H M N S V P
h-IL17B 93 S N K R S L S P W G Y S I N H O P S R I P V D L P E A R C L C L G C V N P F T M Q E D R S M V S V P
h-IL17C 101 T H Q R S I S P W R Y R V D T O E D R Y P O K L A F A E C L R G C I D A R T G R E T A A L N S V R
h-IL17D 86 T N L R S V S P W A Y R I S Y D P A R Y P R Y L P E A Y C L C R G C L T G L F G E E D V R F R S A P
h-IL17E 82 L N S R A I S P W R Y E L D R L N R L P O D L Y H A R C L C P H C V S L O T G S H M D P R G N S E
h-IL17F 74 I E S R S T S P W N Y T V T W D P N R Y P S E V V O A O C R N L G C I N A O G K E D I S M N S V P

h-IL17 115 I O Q E I L V L R R E P P H C P N S F R L E K I L Y S V G C T C V T P I V H H V A
h-IL17B 143 V F S O V P V R R R L C P P P P R T G P C R O R A V M E T I A V G C T C I F
h-IL17C 151 L L O S L L V L R R R P C S R D G S G L P T P G A F A F H T E F I H V P V G C T C V L P R S V
h-IL17D 136 V Y M P T V V L R R T P A C A G G R S V Y T E A Y V T I P V G C T C V P E P E K D A D
h-IL17E 132 L L Y H N O T V F Y R R P C H G E K G T H K G Y C L E R R L Y R V S L A C V C V R P R V M G
h-IL17F 123 I O Q E T L V V R R K H O G C S V S F O L E K V L V T V G C T C V T P V I H H V O

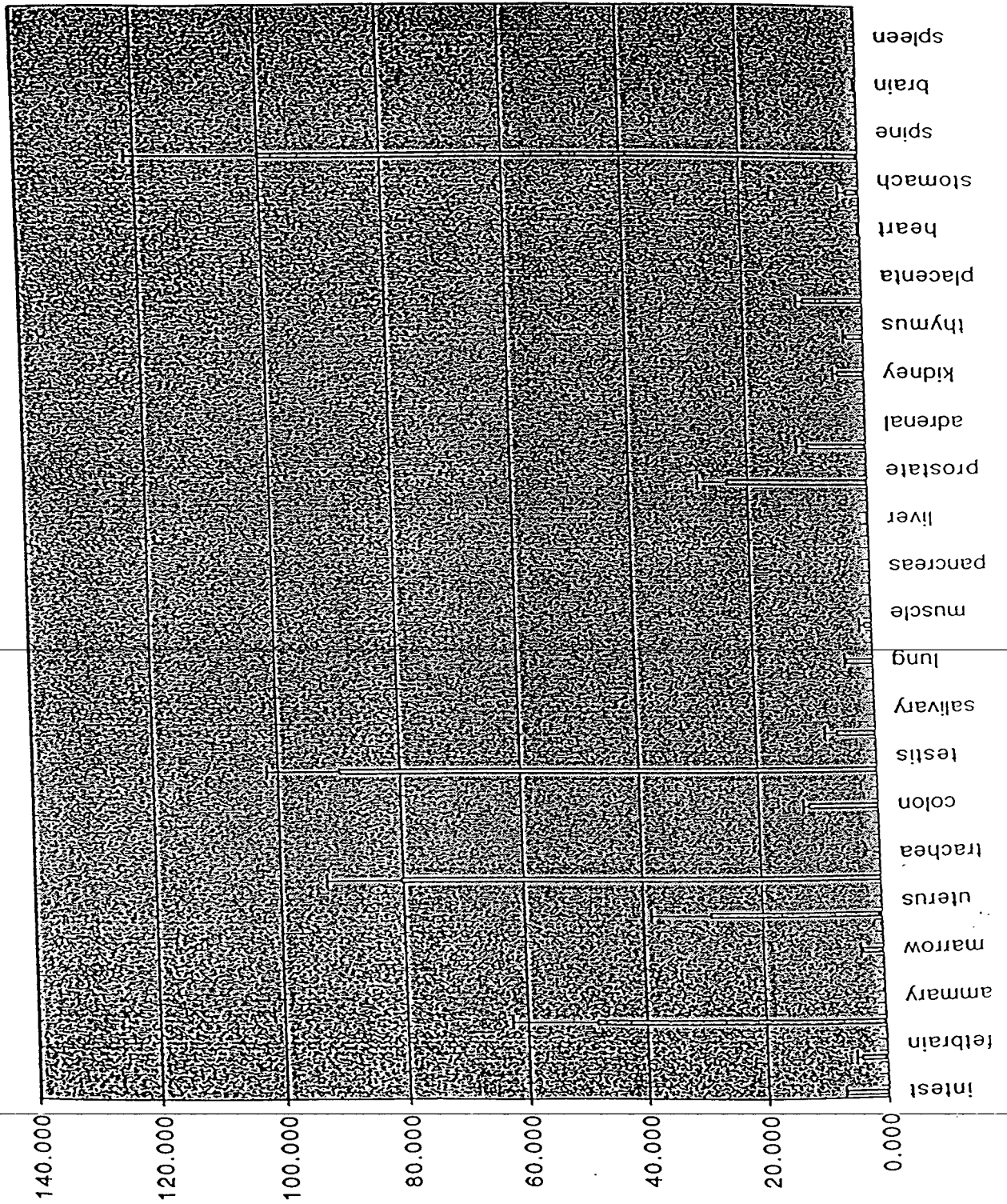
h-IL17D 179 S I N S S I O K O G A K L L L G P N D A P A G P X

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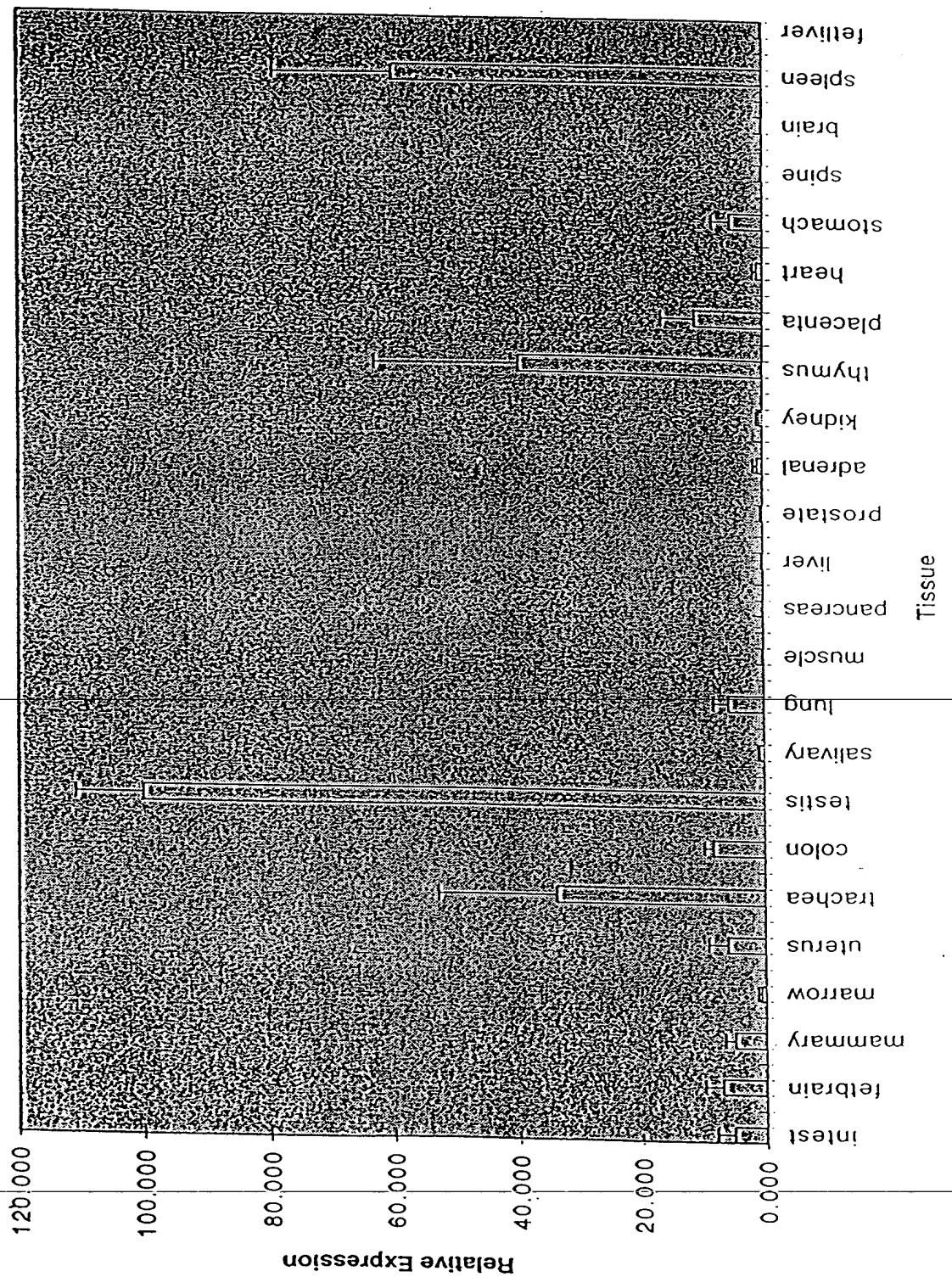
FIGURE 20

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IL17B distribution



IL17C Distribution



IL17D Distribution

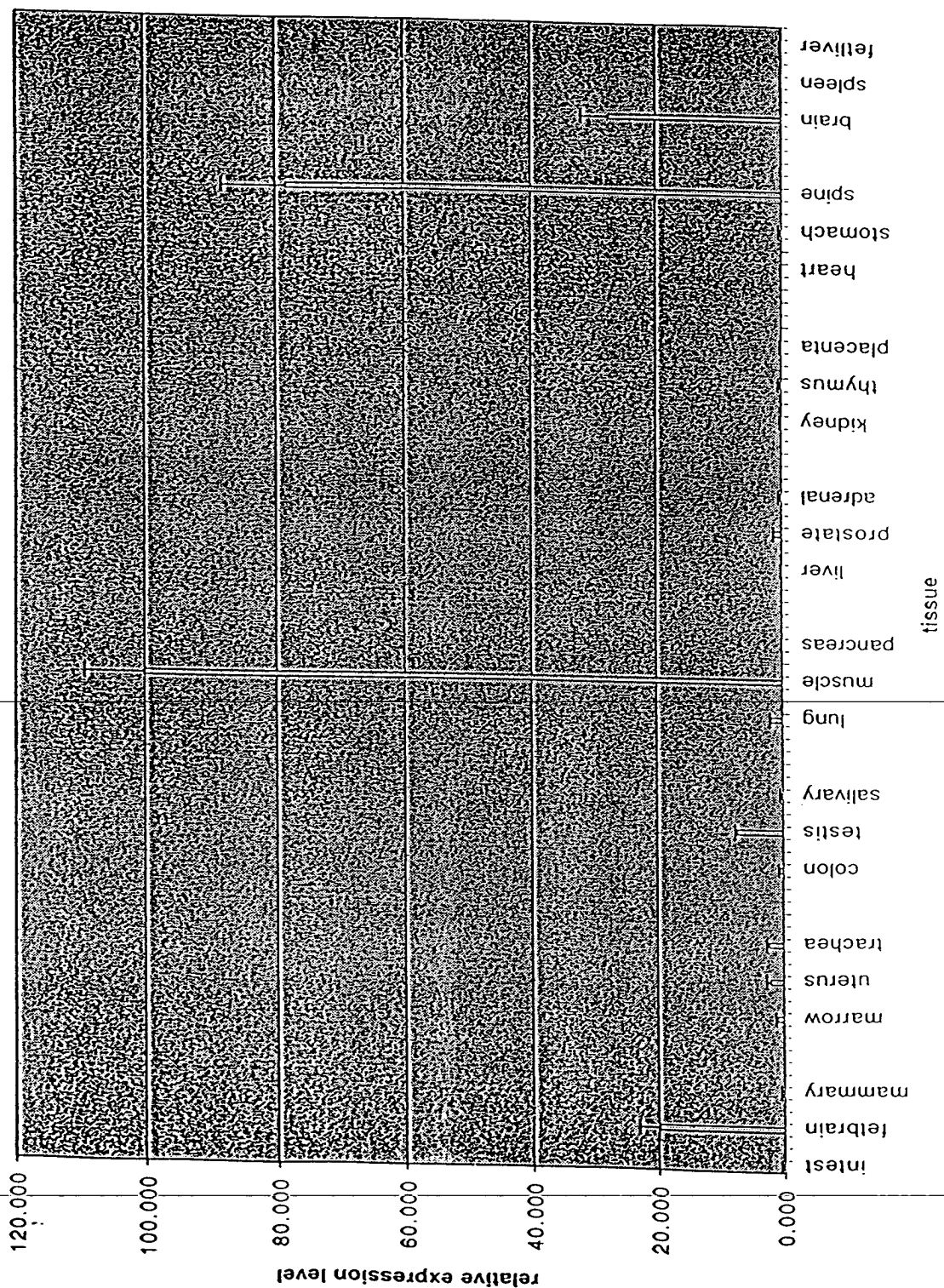


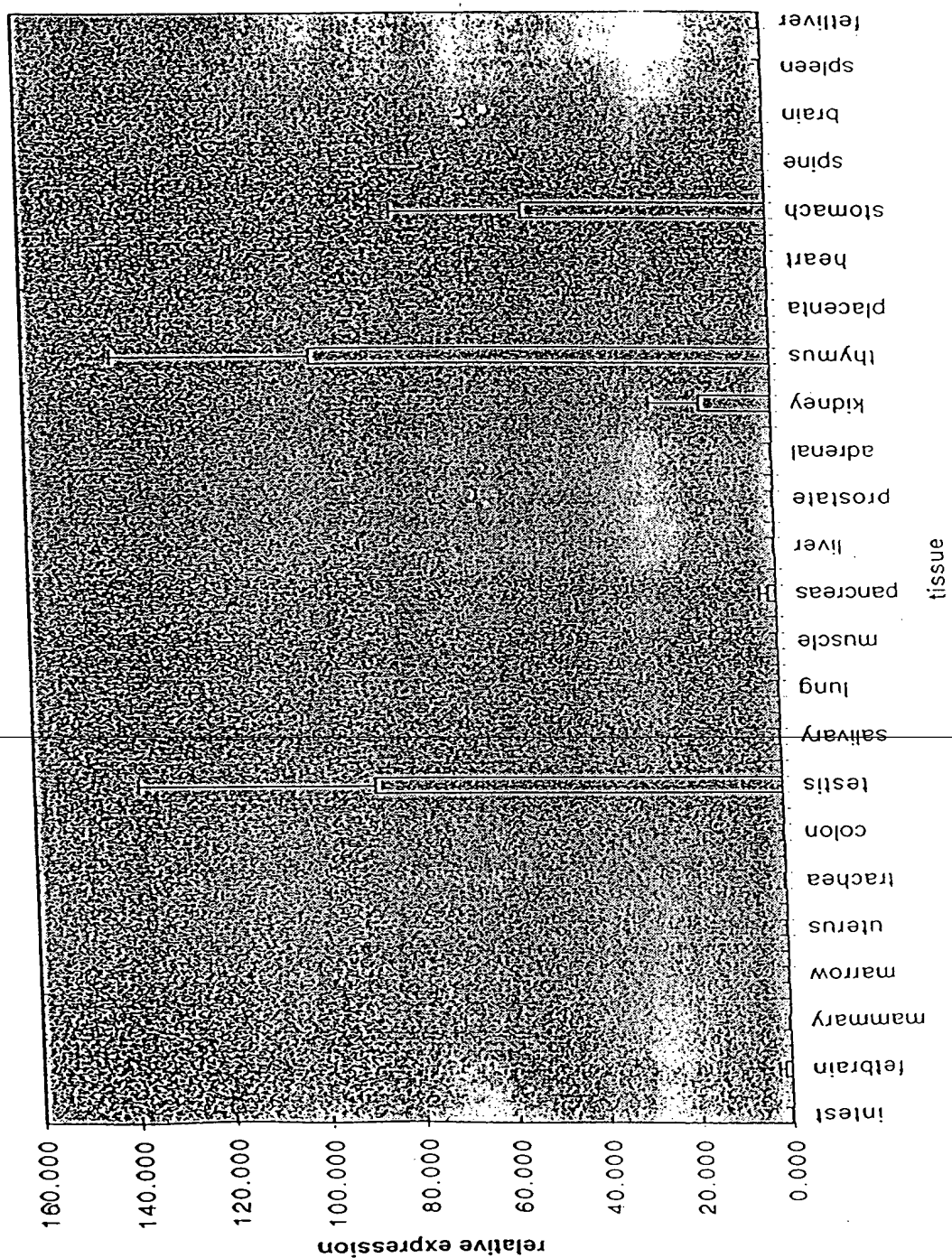
FIGURE 23

FOOT" 250000

Brain	1
heart	
kidney	1
liver	
lung	
colon	
marrow	
intestine	
spleen	
stomach	
thymus	1
prostate	
muscle	
testis	1
uterus	
fetal brain	
fetal liver	
spinal chord	1
placenta	
adrenal	
pancreas	
salivary	
trachea	1
mammary	

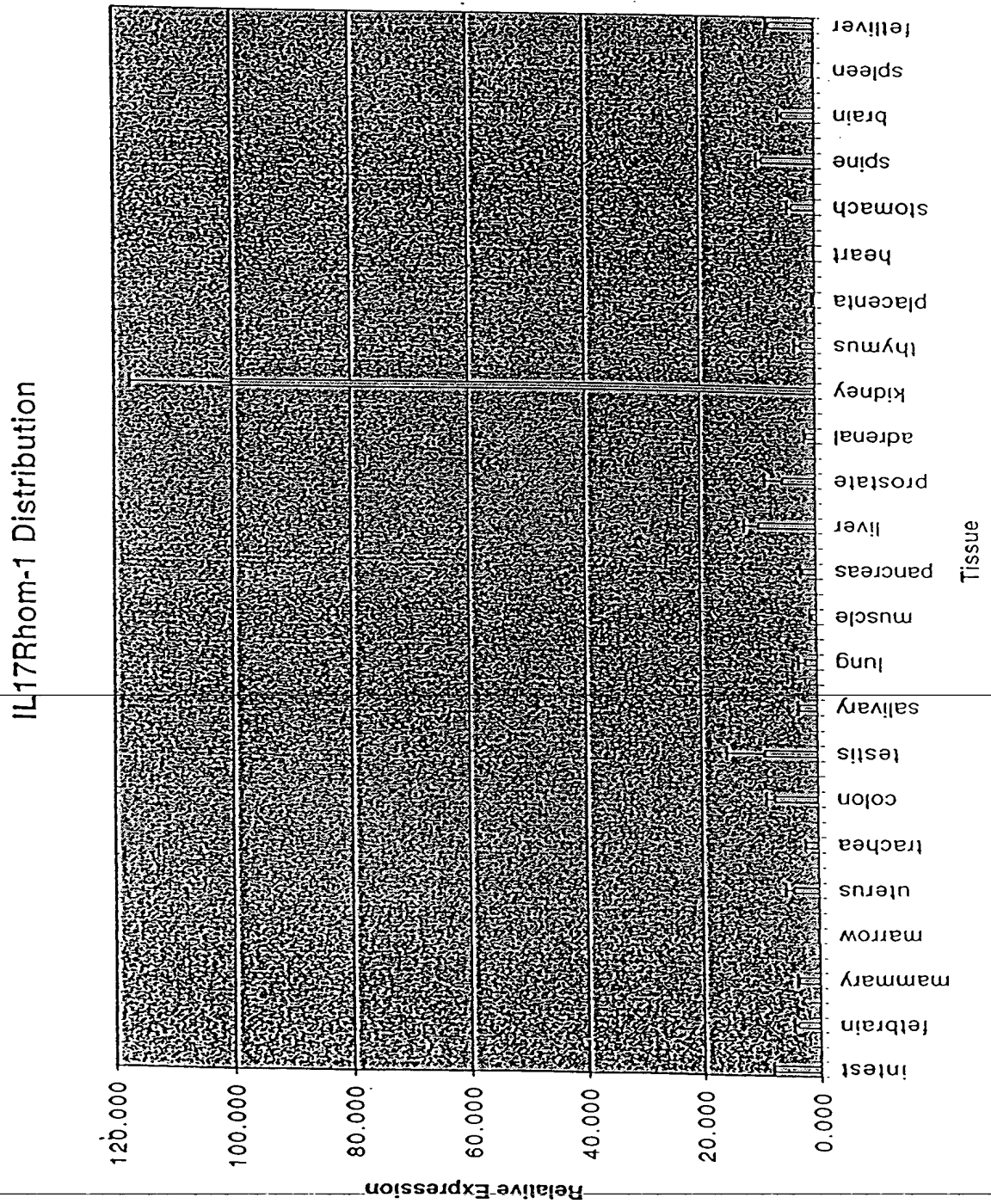
FIGURE 24

IL17 F Distribution



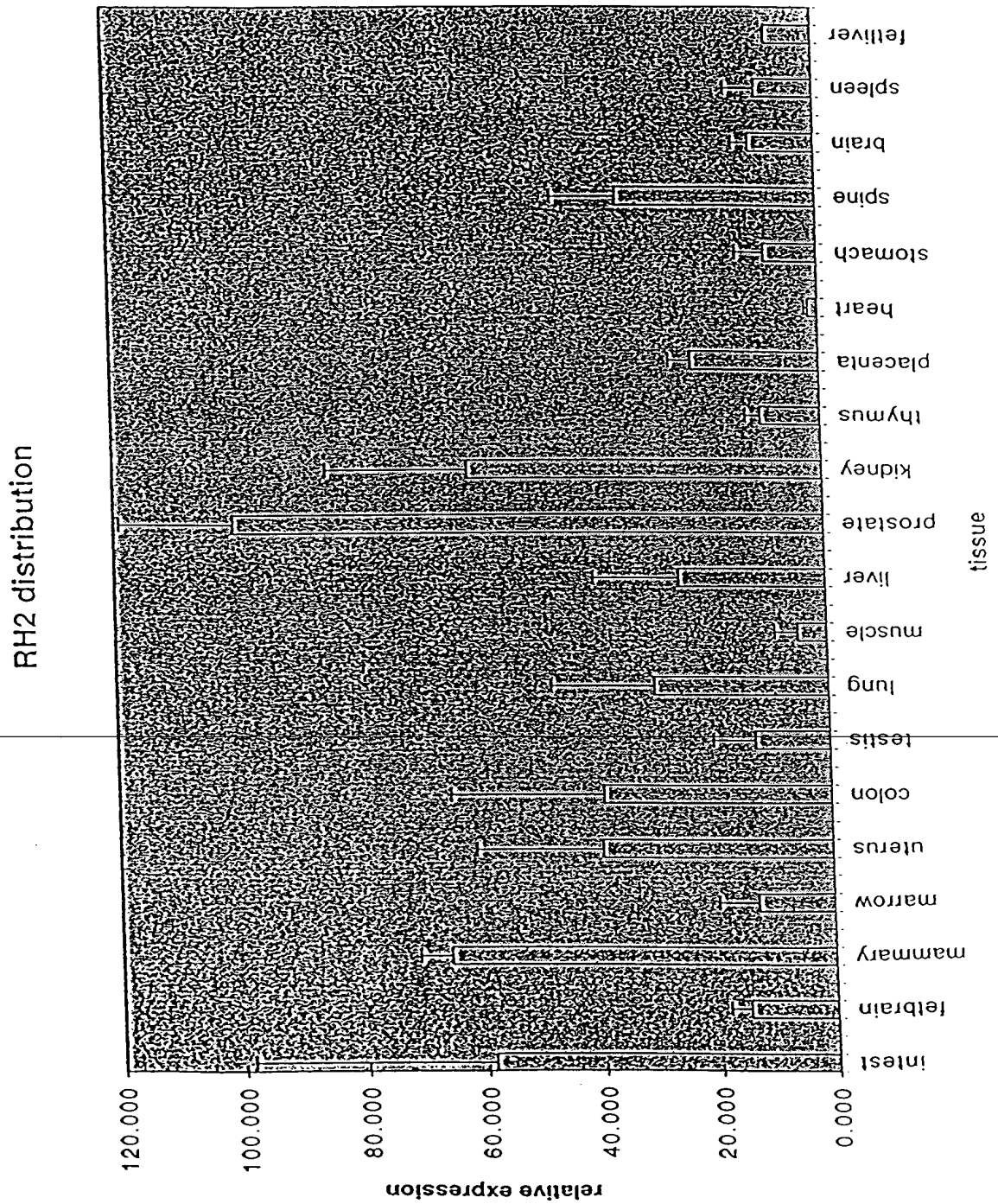
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FIGURE 25



T00501-75100001

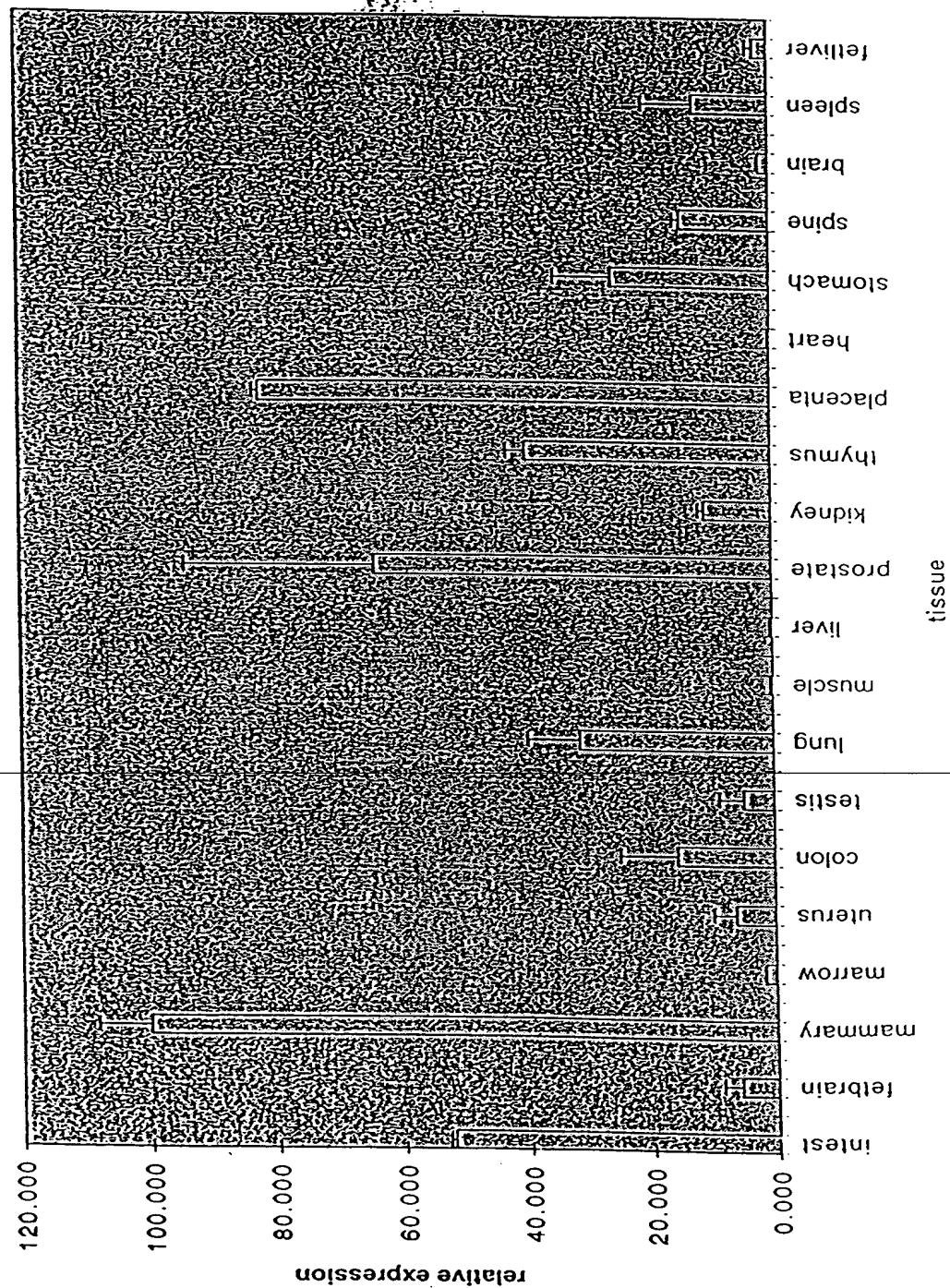
FIGURE 26



FOOET" /STFOOOOT

FIGURE 27

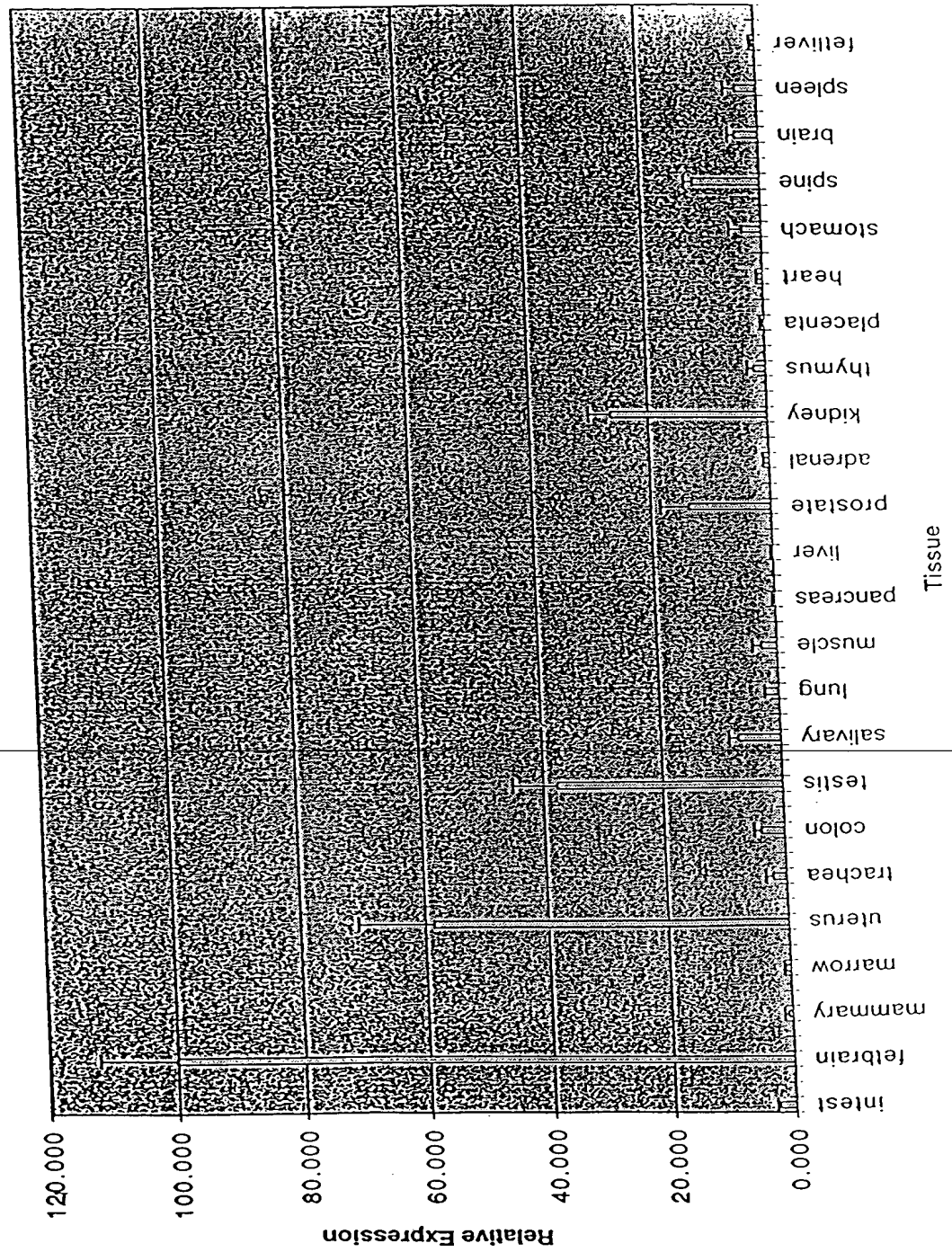
RH3 distribution



T00E0T" 45T0000T

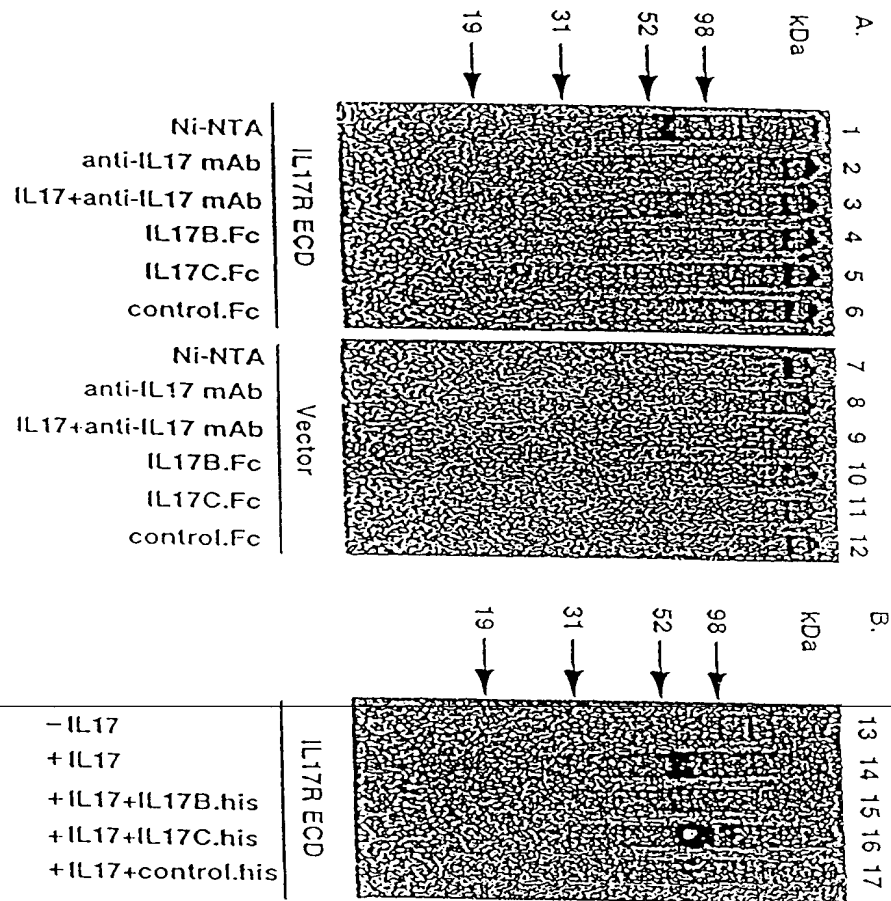
FIGURE 28

IL17 RH4 distribution



100000 45100000

FIGURE 29



10000157 103001

FIGURE 30

h-IL17 1 - - - - - M T P G K T S L V S L L L L S L E A I V K A G I T I P R - - - - -
h-IL17B 1 - - - - M D W P H N L L F L L T I S I F L G L G Q P R S P K S K R K G Q G R P G P - - - - -
h-IL17C 1 - - - - M T L L P G L L F L T W L H T C L A H H D P S L R G H P H S H G T P H C Y S A E E L P L G
h-IL17E 1 M R E R P R L G E D S S L I S L F L Q V V A F L A M V M G T H T Y S H W P S C C P - - - - -

h-IL17 30 - - - - - N P G C P N S E D K N F P R T V M V N L N I H N R N T N T N P K R - - - - -
h-IL17B 39 A P G P H Q V P L D L V S R M K P Y A R M E E Y E R N I E E M V A Q L R N S S E L A O R K C E V N
h-IL17C 47 A P P H L L A R G A K W G O A L P V A L V S S L E A A S H R G R H E R P S A T T O C P V L R P E E
h-IL17E 42 - - - - - S K G Q D T S E E L L R W S T V P V P P L E P A R P N R H P E S C R A S E

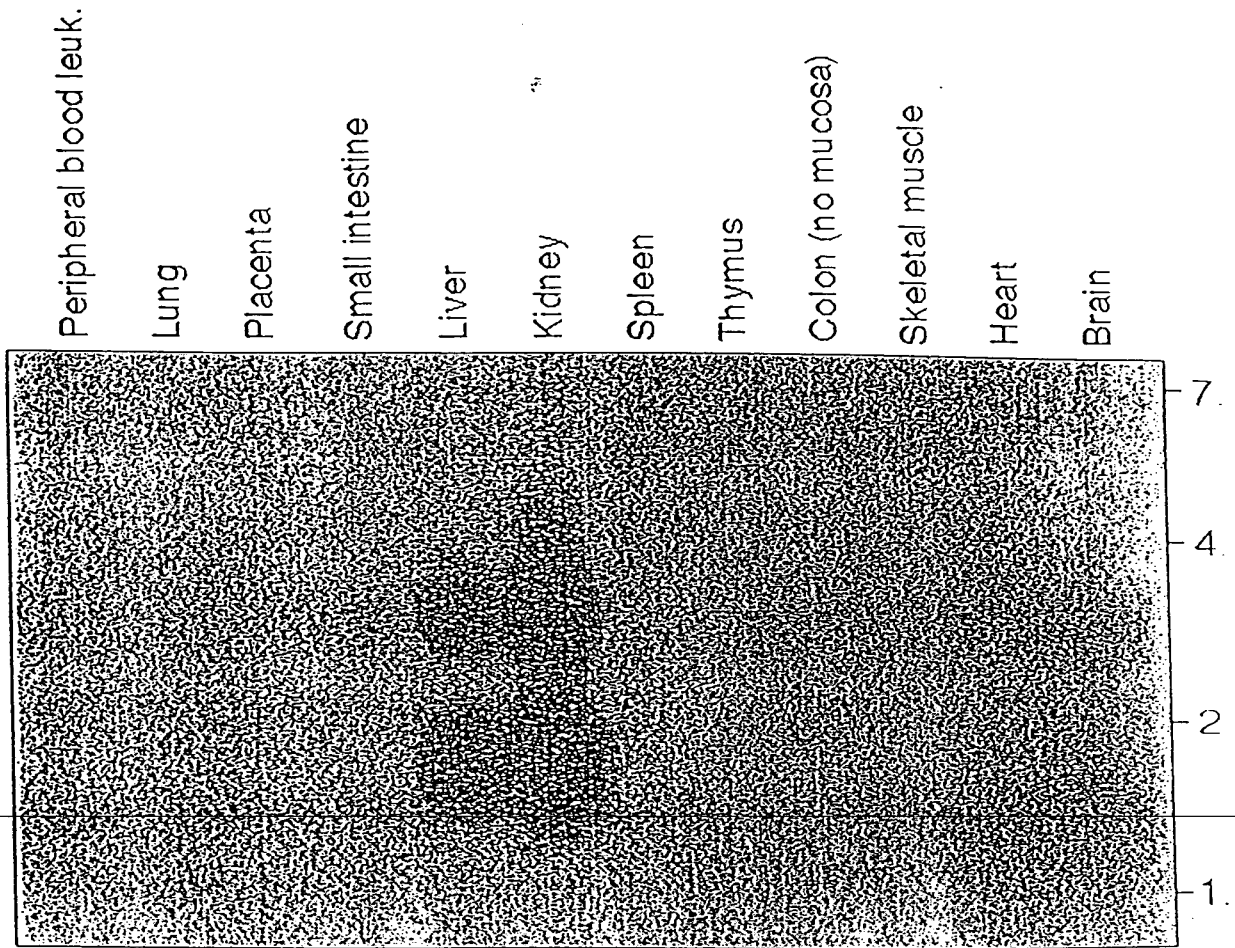
h-IL17 63 - S S D Y Y N R S T S P W N L H R N E D P E R Y P S V I W E A K C R H L G C I N A D G - - N V D Y
h-IL17B 69 Q L W M S N K R S L S P W G Y S I N H D P S R I P V D L P E A R C L C L G C V N P F T M O E D R S
h-IL17C 97 L E A D T H Q R S I S P W R Y R V D T D E D R Y P Q K L A F A E C L C R G C I D A R T G - R E T A
h-IL17E 79 - D G P L N S R A I S P W R Y E L D R D L N R L P Q D L Y H A R C L C P H C V S L Q T G S H M D P

h-IL17 110 M N S V P I Q O E I L V L R R E - - - - - P P H C P N S F R L E K I L V S V G C T C V T P
h-IL17B 139 V S V P V F S Q V P V R R R L C P P P - - - - - P R T G P C R Q R A V M E T I A V G C T C I F -
h-IL17C 146 L N S V R L L Q S L L V L R R R P C S R D G S G L P T P G A F A F H T E F I H V P V G C T C V L P
h-IL17E 128 G N S E L L Y H N Q T V F Y R R P C H G E K - - - G T H K G Y C L E R R L Y R V S L A C V C V R P

h-IL17 151 V H H V A
h-IL17C 196 S V - - -
h-IL17E 175 V M G - -

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FIGURE 31A



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FIGURE 31B

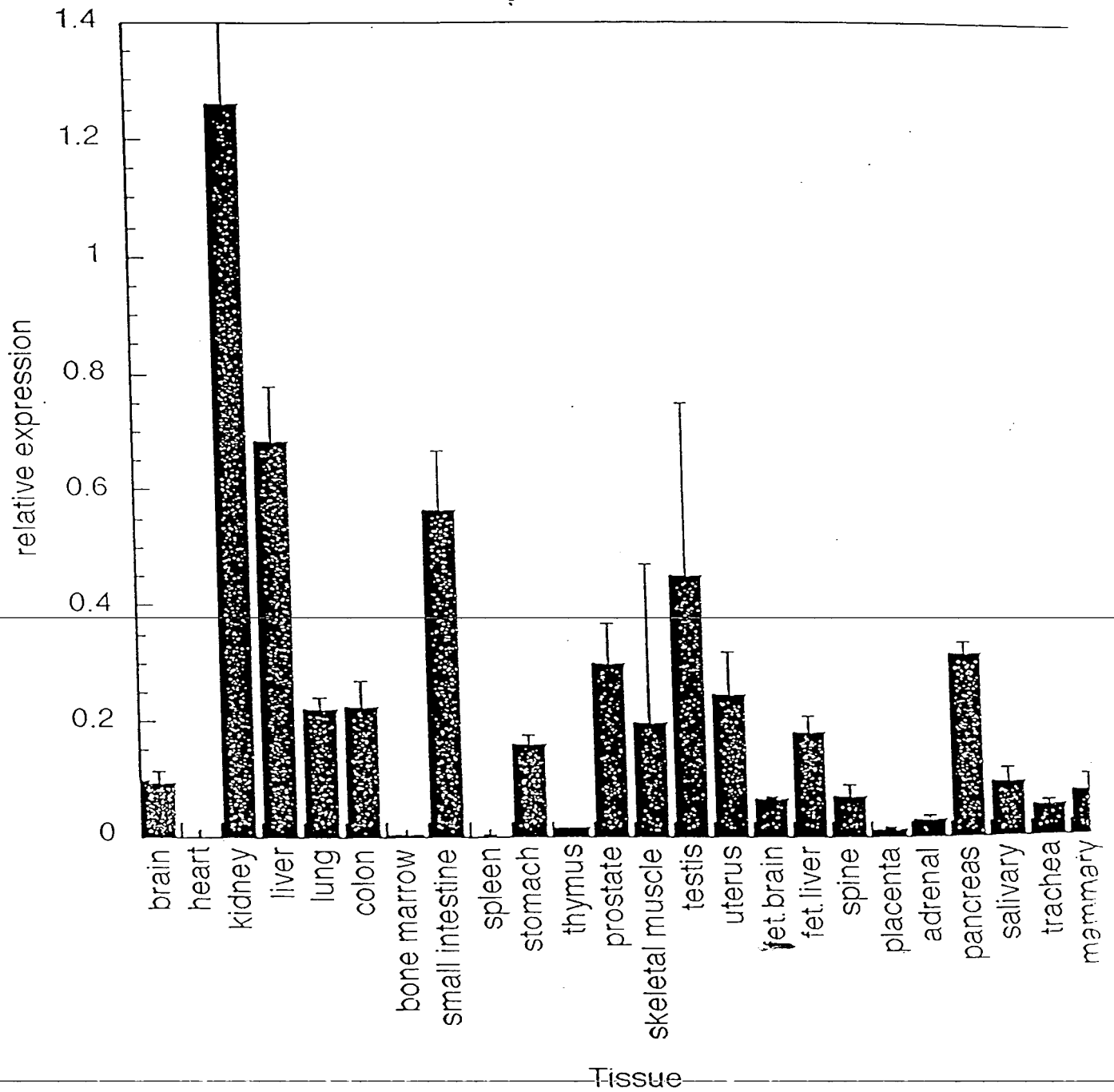


FIGURE 32A

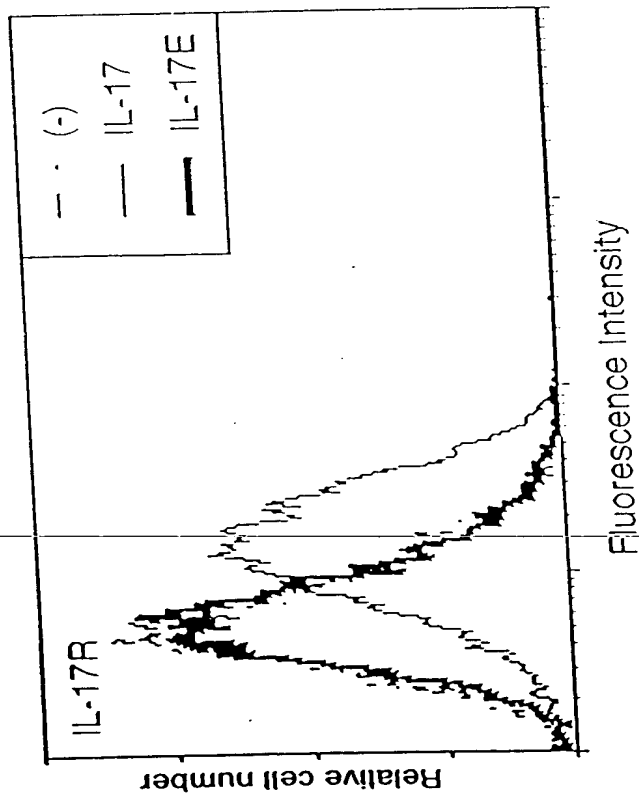
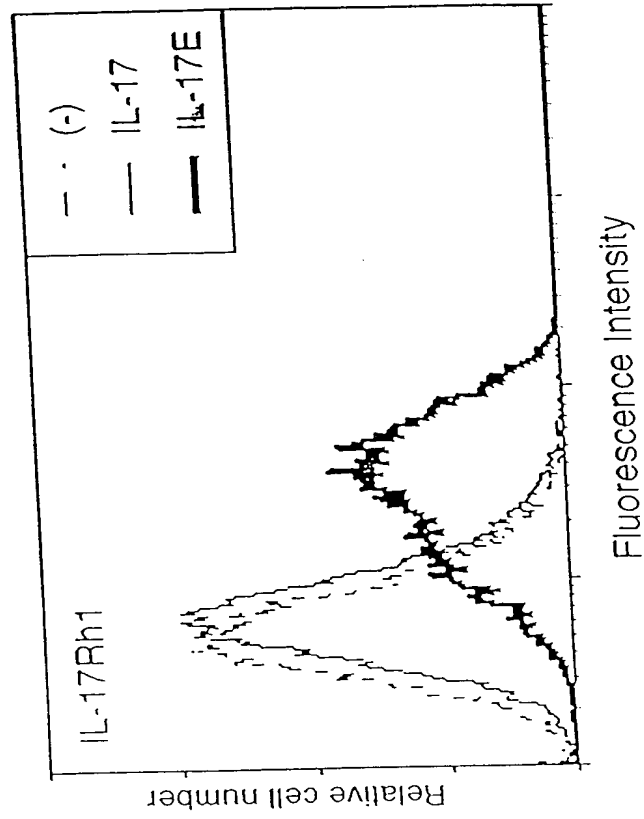
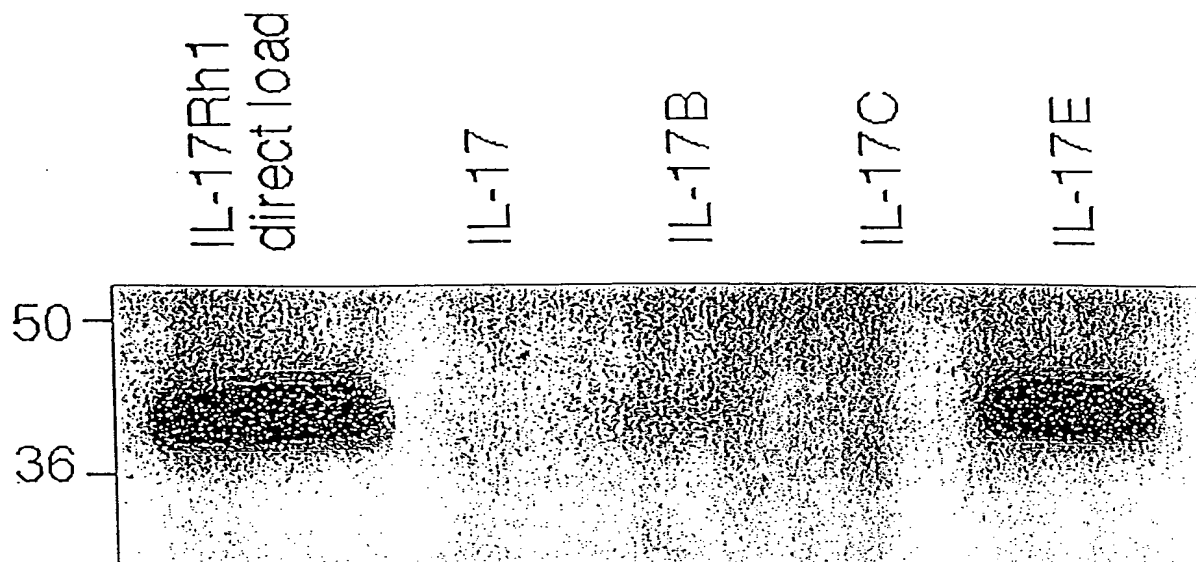


FIGURE 32B



FOOT" /5FOOOT

FIGURE 33

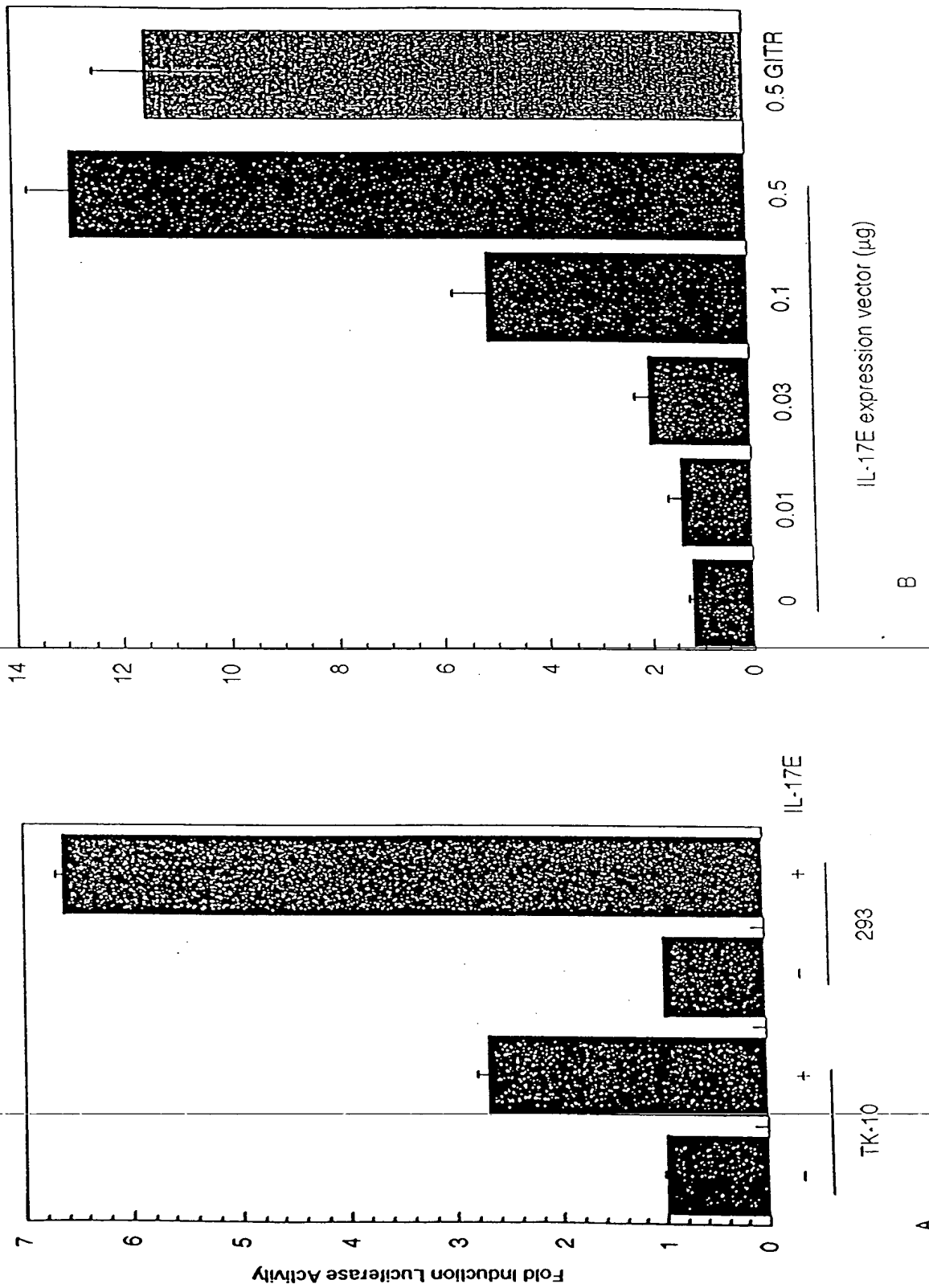


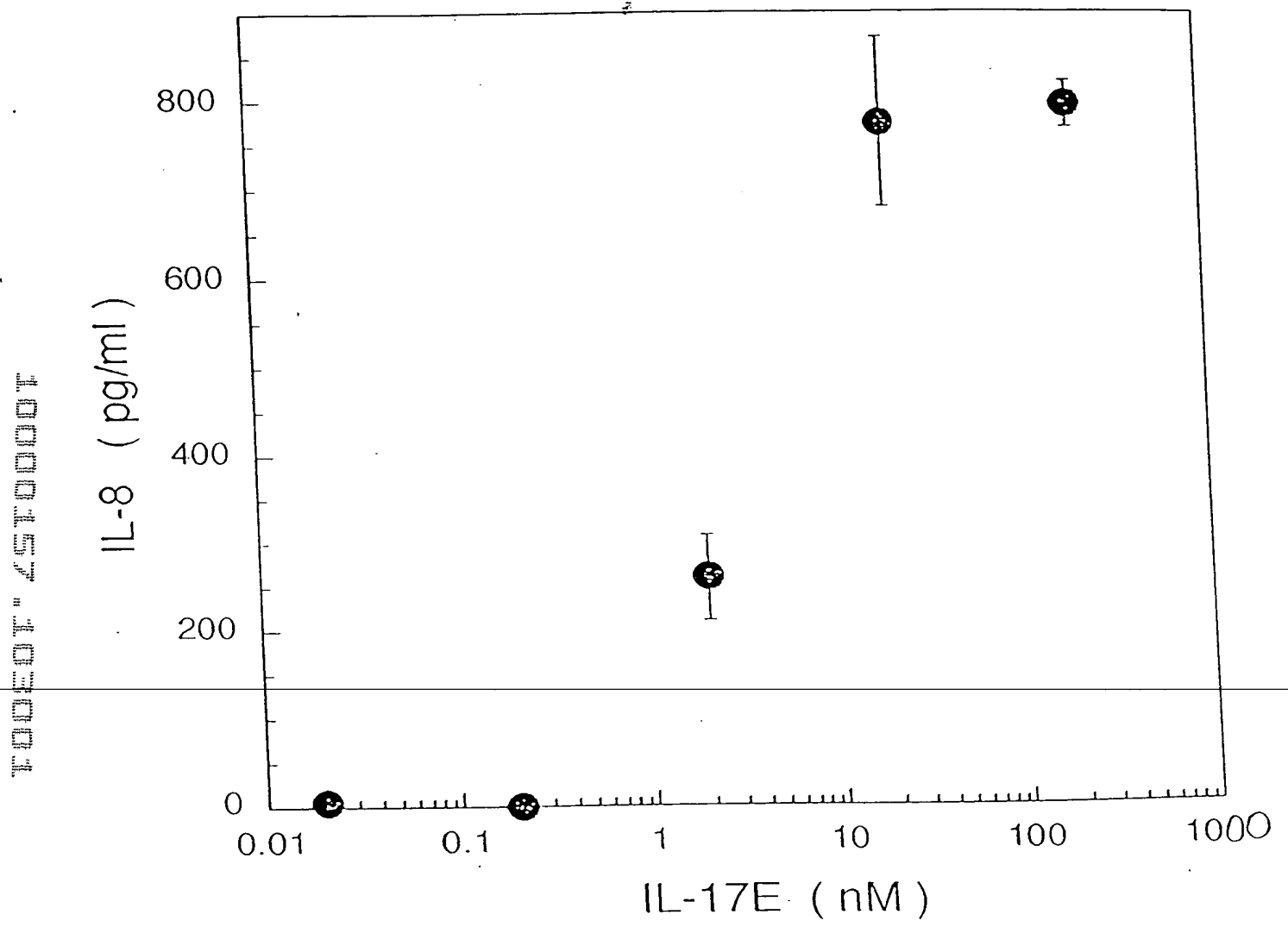
FIGURE 34

FIGURE 35

IL-17 family of cytokines has complex pattern
of overlapping receptor-ligand specificities

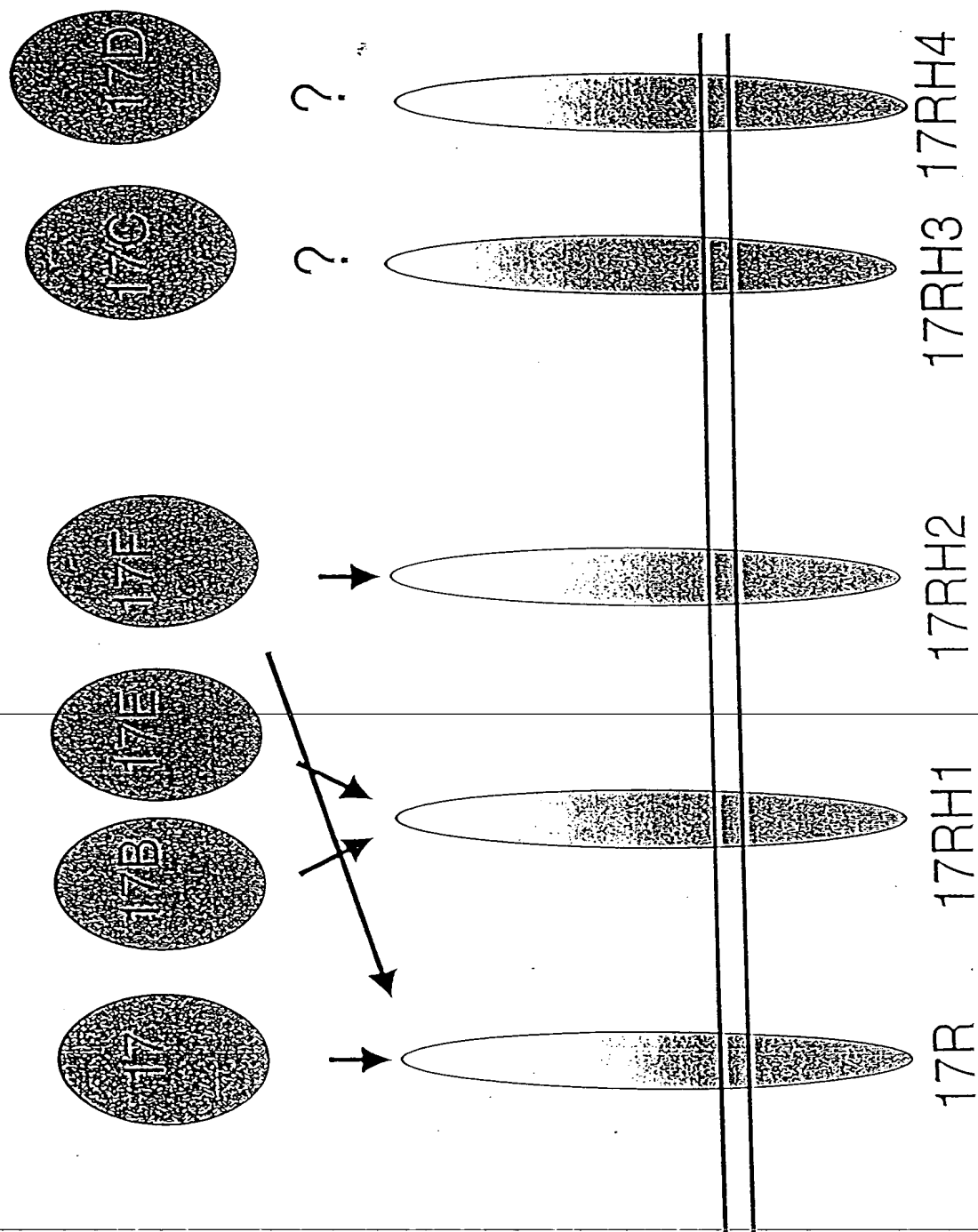


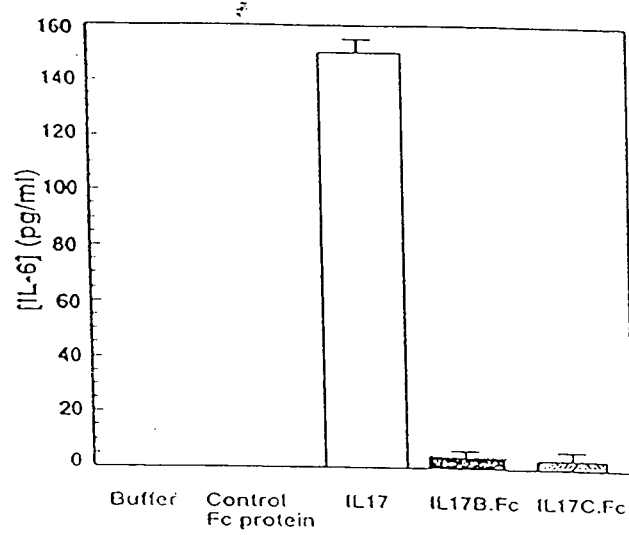
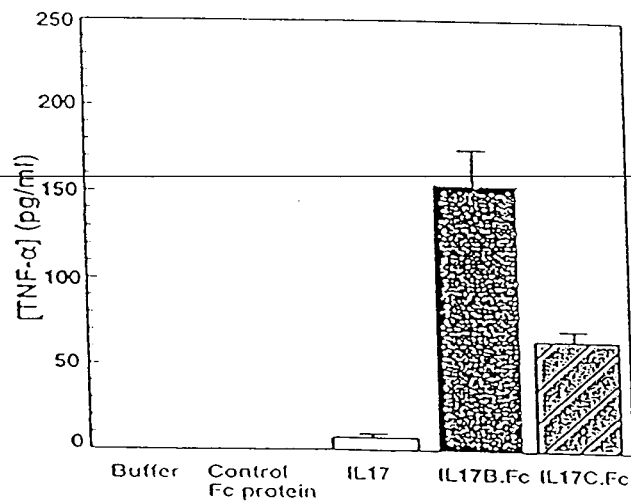
FIGURE 36**A. HFF cells****B. THP1 cells**

FIGURE 37

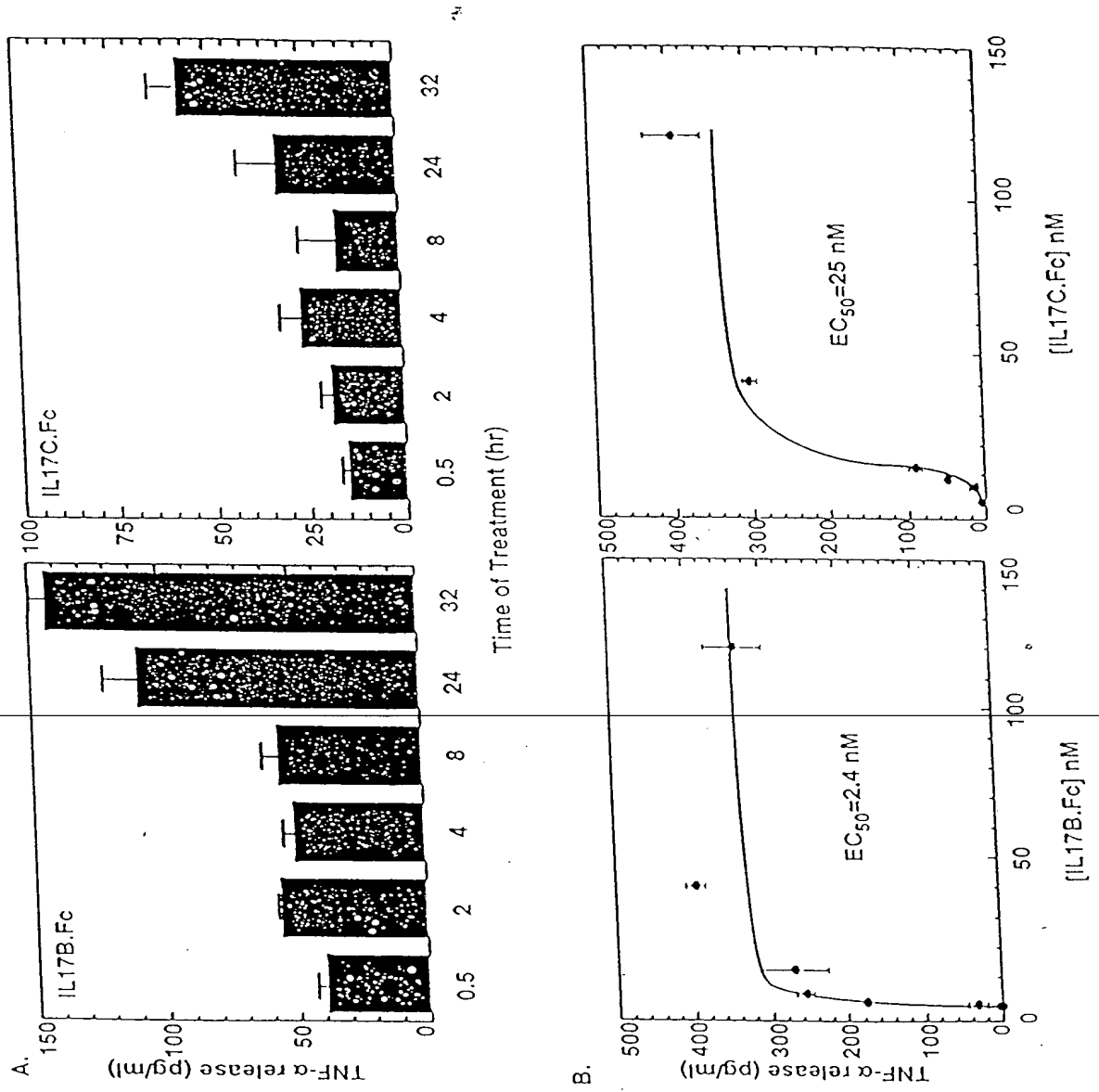
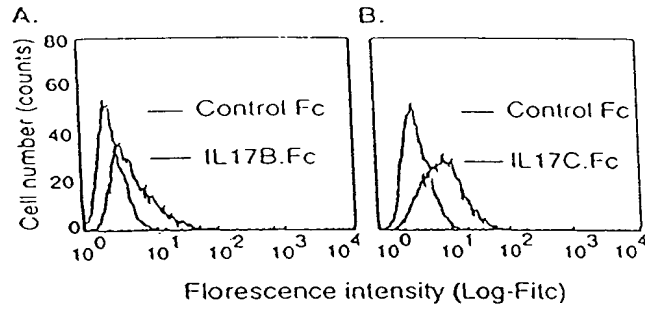


FIGURE 38



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FIGURE 39

IL-17 induces breakdown and inhibits synthesis of cartilage matrix

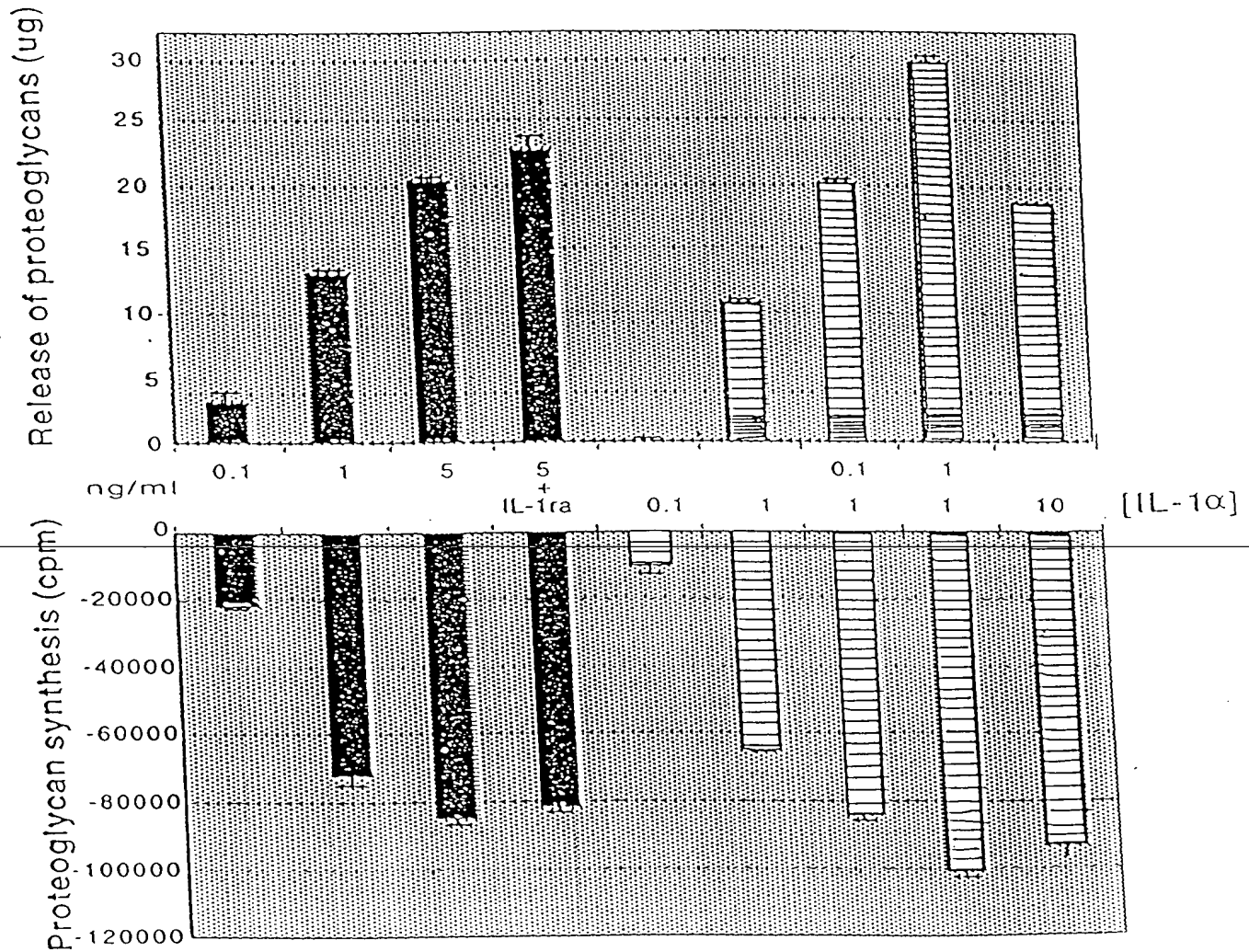
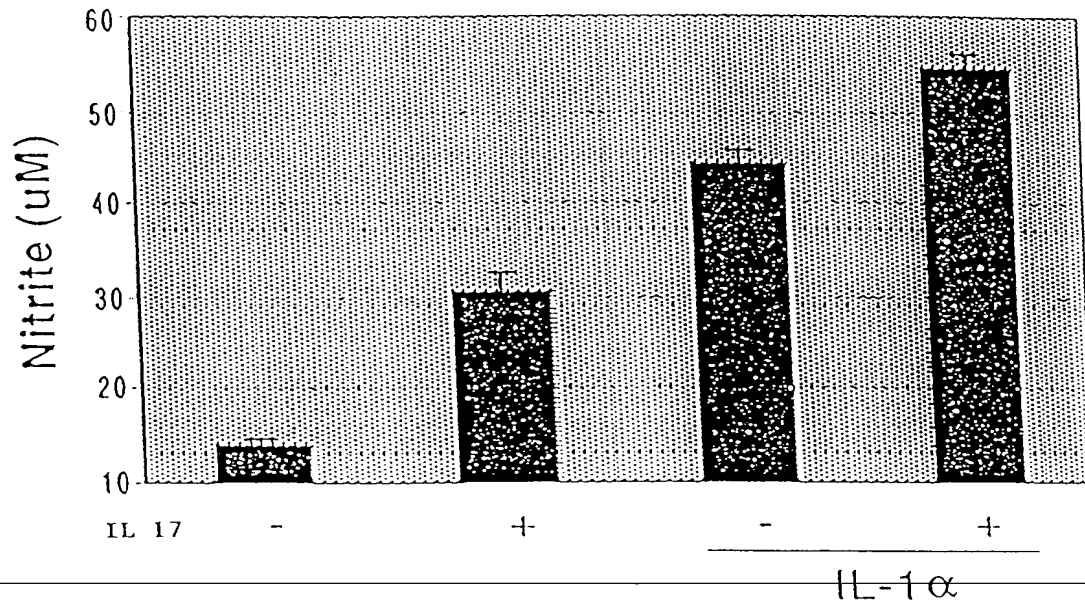


FIGURE 40

IL 17 increases basal and
IL-1 α -induced nitric oxide release

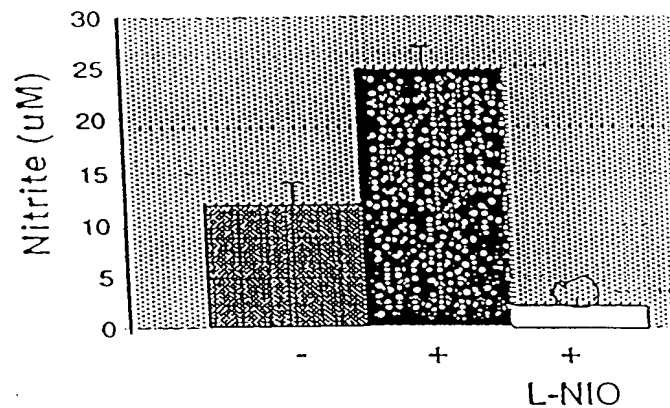


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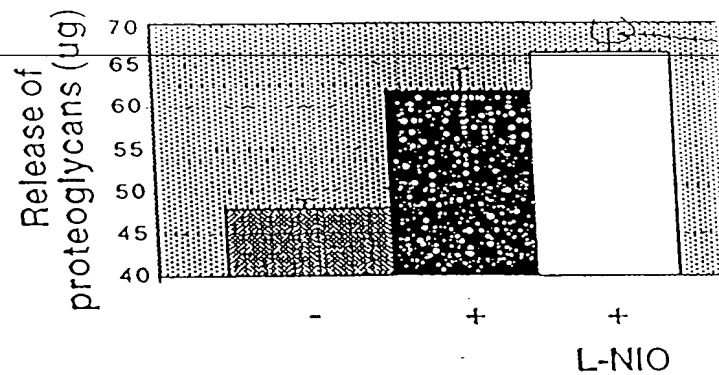
FIGURE 41

Inhibition of nitric oxide release does not block the detrimental effects of IL-17 on matrix breakdown or synthesis

A.



B.



C.

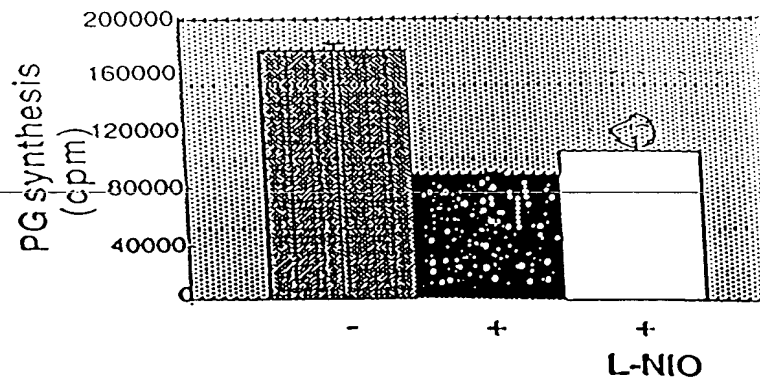
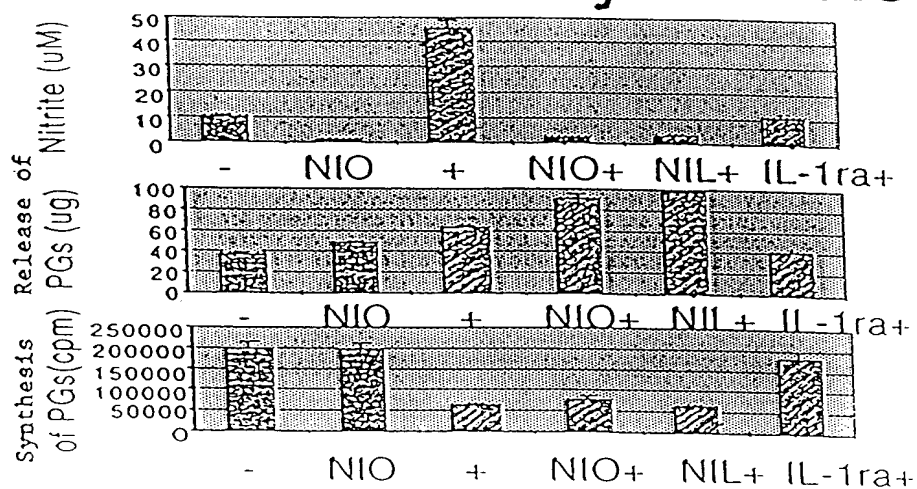


FIGURE 42

INHIBITION of NO release enhances
 IL-1 α -induced matrix breakdown
 but not matrix synthesis



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FIGURE 43

IL-17C

detrimental effects on articular cartilage

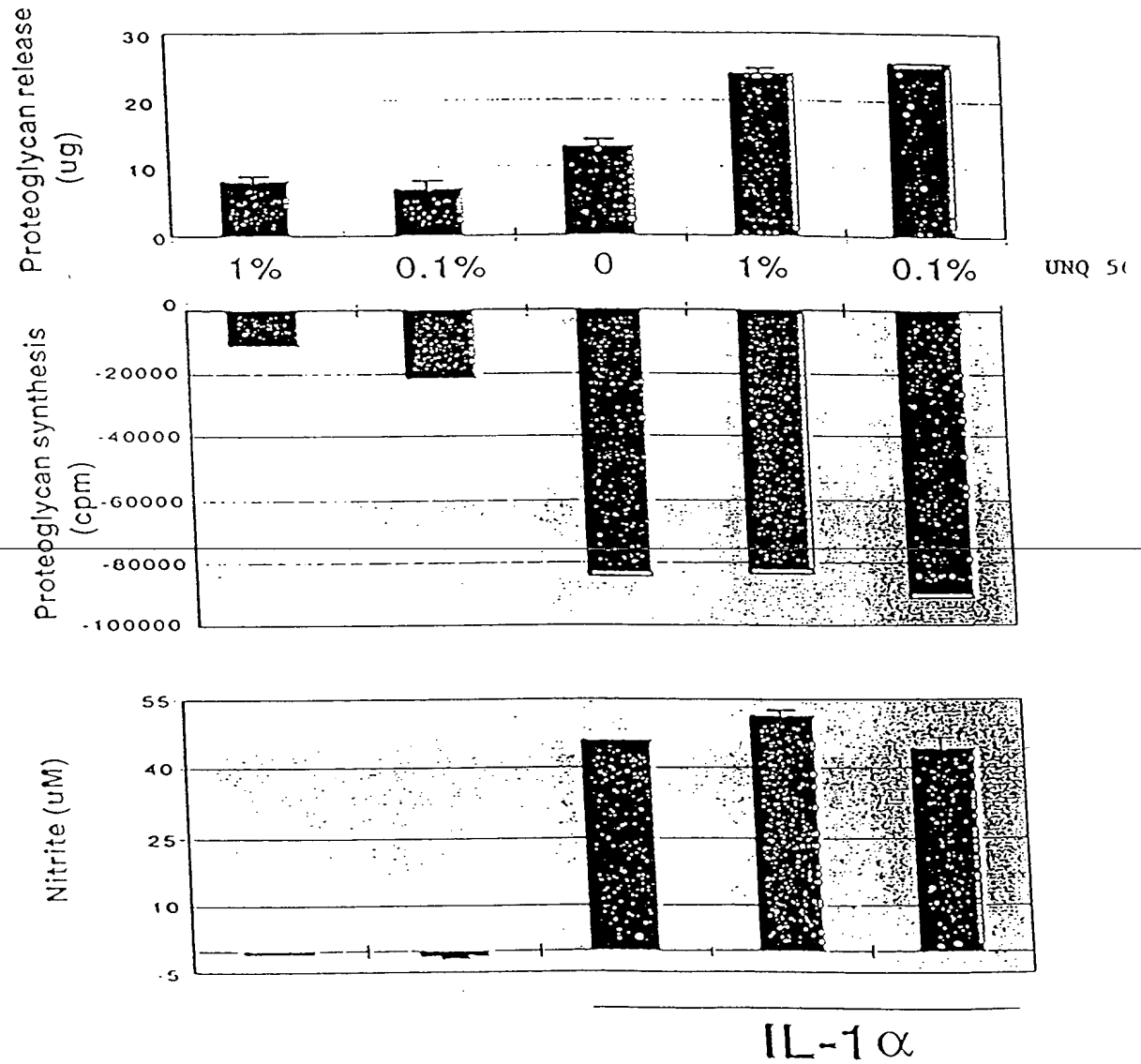
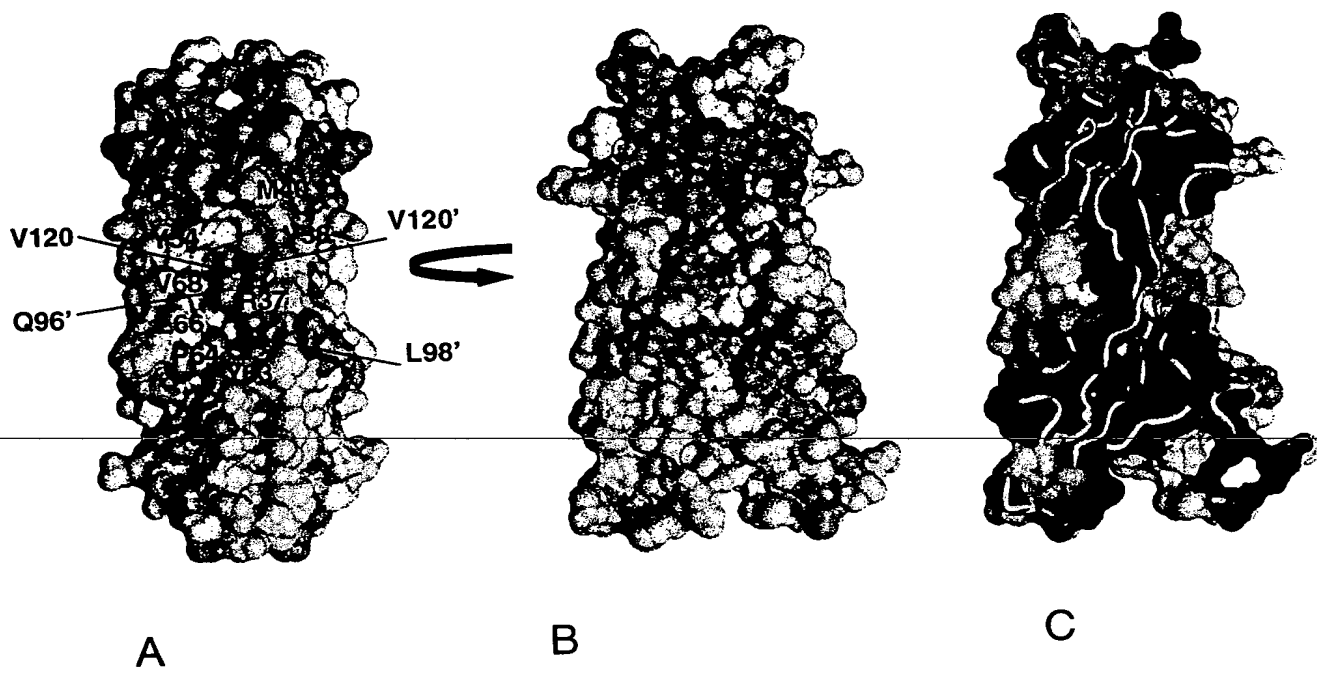


FIGURE 51



IL-17E is highly conserved between human and mouse

FIGURE 53

mL-17E	1	-----	VAFLAM	IVGTH	IVSLRIQEGC	SHL	PSCCPS
nL-17E	1	MRERPR	LGEDSS	LI SLFLQV	VAFLAM	VMGTH	-----YSHWPSCCPS
mL-17E	35	KEQ	EPPE	EWKWS	ASVSP	PEPL	LSHTHA
nL-17E	43	KGQ	DTSE	ELLRWS	TVPPV	PEPL	EPARPNRHP
							ESCRASE
							DGGLNSRAISPWRY
mL-17E	85	ELDR	DLNR	VPQ	DLYHAR	CLCPH	CVSLQTGSHMDPL
nL-17E	93	ELDR	DLNR	LPQ	DLYHAR	CLCPH	CVSLQTGSHMDPR
							GNSTVP
							LYHNQTVFYR
mL-17E	135	RPCH	GGE	STHR	RK	CLERR	LYRVSLACVCVRPRVMA
nL-17E	143	RPCH	GGE	STHK	GK	CLERR	LYRVSLACVCVRPRVMG

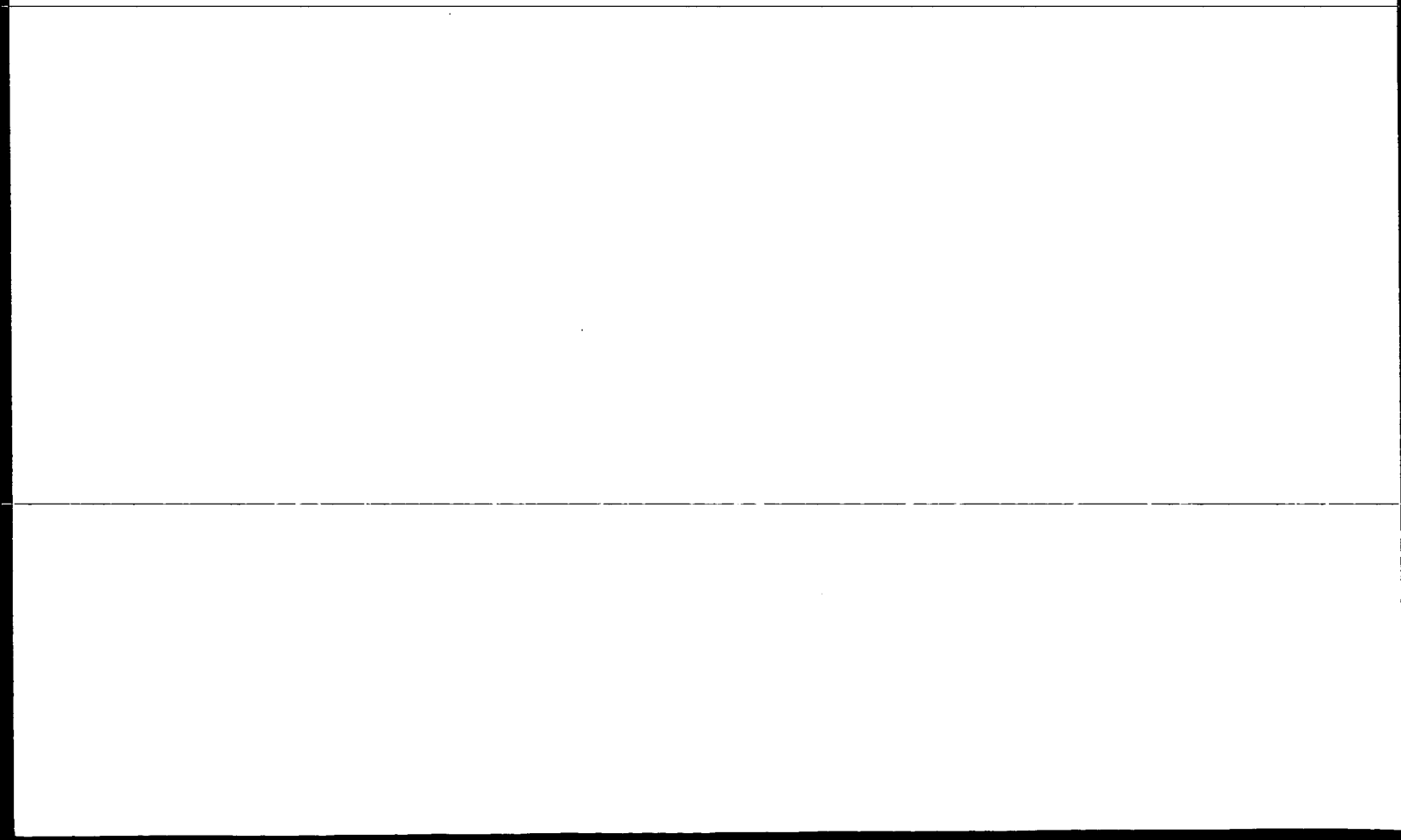


FIGURE 8

MLVAGFLLALPPSWAAGAPRAGRPARPRGCAADRPEELLEQLYGRIAGVLSAFHHTLQLGPREQARNASC
PAGGRPGRDRFRPPTNLRVSPWAYRISYDPARYPRYLPEAYCLCRGCLTGLFGCEEDVRFRSAPVYMPTVV
LR RTPACAGGRSVYTEAYVTIPVGCTCVPEPEKDADSINSSIDKQAKLLLGPNDAPAGP

Signal peptide:	Amino acids 1-15
N-glycosylation sites:	Amino acids 68-72;181-185
Tyrosine kinase phosphorylation site:	Amino acids 97-106
N-myristoylation sites:	Amino acids 17-23;49-55;74-80; 118-124
Amidation site:	Amino acids 21-25

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FIGURE 4

MTLLPGLLFLTWLHTCLAHHDPSLRGHPHSHGTPHCYSAEELPLGQAPPHLLARGAKWGQALPVALVSSLE
AASHRGRHERPSATTQCPVLRPEEVLEADTHQRSISPWRYRVDTDEDYPQKLAF AECLCRGCIDARTGRE
TAALNSVRLLQSLLVLRRRPCSRDGSGGLPTPGAF AFHTEFIHVPVGCTCVLPRSV

Signal peptide:	Amino acids 1-18
Tyrosine kinase phosphorylation site:	Amino acids 112-121
N-myristoylation sites:	Amino acids 32-38;55-61;133-139
Leucine zipper pattern:	Amino acids 3-25
Homologous region to IL-17:	Amino acids 99-195

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FIGURE 6

MRERPRLGEDSSLISLFLQVVAFLAMVMGTHYSHWPSCCPKQDTSEELLRWSTVPVPPLEPARPNRHP
ESCRASEDGPLNSRAISPWRYELDRDLNRLPQDLYHARCLCPHCVSLQTGSHMDPRGNSELLYHNQTVFYR
RPCHGEKGTHTKGYCLERRLYRVSLACVCVRPRVMG

Signal peptide:

Amino acids 1-32

N-glycosylation site:

Amino acids 136-140

Tyrosine kinase phosphorylation site:

Amino acids 127-135

N-myristoylation sites:

Amino acids 44-50;150-156

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FIGURE 7

ATGCTGGTAGCCGGCTTCCTGCTGGCGCTGCCGCCGAGCTGGGCCGCGGGCGCCCCAGGGCGGGCAGGCG
CCCCGCGCGGGCCGCGGGGCTGCGCGGACCGGCCGGAGGAGCTACTGGAGCAGCTGTACGGGCGCCTGGCGG
CCGGCGTGCTCAGTGCCTTCCACCACACGCTGCAGCTGGGGCCGCGTGAGCAGGCGCGCAACGCGAGCTGC
CCGGCAGGGGGCAGGCCCCGGCGACCGCCGCTTCCGGCCGCCCCACCAACCTGCGCAGCGTGTCGCCCTGGGC
CTACAGAATCTCCTACGACCCGGCGAGGTACCCAGGTACCTGCCTGAAGCCTACTGCCTGTGCCGGGGCT
GCCTGACCGGGGCTGTTTCGGCGAGGAGGACGTGCGCTTCCGCAGCGCCCCTGTCTACATGCCCACCGTCGTC
CTGCGCCGCACCCCCGCTGCGCCGGCGGCCGTTCCGTCTACACCGAGGCCTACGTCAACCATCCCCGTGGG
CTGCACCTGCGTCCCCGAGCCGGAGAAAGGACGCGACAGCATCAACTCCAGCATCGACAAACAGGGCGCCA
AGCTCCTGCTGGGCCCCAACGACGCGCCCGCTGGCCCCCTGAGGCCGCTCCTGCCCCGGGAGGTCTCCCCGG
CCCGCATCCCCGAGGCGCCCAAGCTGGAGCCGCTGGAGGGCTCGGTGCGGACCTCTGAAGAGAGTGCACC
GAGCAAACCAAGTGCCGGAGCACCAGCGCCGCTTTCCATGGAGACTCGTAAGCAGCTTCATCTGACACGG
GCATCCCTGGCTTGCTTTTAGCTACAAGCAAGCAGCGTGCTGGAAGCTGATGGGAAACGACCCGGCACGG
GCATCCTGTGTGCGGCCCGCATGGAGGGTTTGGAAAAGTTCACGGAGGCTCCCTGAGGAGCCTCTCAGATC
GGCTGCTGCGGGTGACGGGCGTGA CTACCGCTGGGTGCTTGCCAAAGAGATAGGGACGCATATGCTTTTT
AAAGCAATCTAAAAATAATAAAGTATAGCGACTATATACCTACTTTTAAATCAACTGTTTTGAATAGA
GGCAGAGCTATTTTATATTATCAAATGAGAGCTACTCTGTTACATTTCTTAACATATAAACATCGTTTTTT
ACTTCTTCTGGTAGAATTTTTTAAAGCATAATTGGAATCCTTGGATAAATTTTGTAGCTGGTACACTCTGG
CCTGGGTCTCTGAATTCAGCCTGTCACCGATGGCTGACTGATGAAATGGACACGTCTCATCTGACCCACTC
TTCCTTCCACTGAAGGTCTTCACGGGCCTCCAGGTGGACCAAAGGGATGCACAGGCGGCTCGCATGCCCCA
GGGCCAGCTAAGAGTTCCAAAGATCTCAGATTTGGTTTTAGTCATGAATACATAAACAGTCTCAAACCTCGC
ACAATTTTTTCCCCCTTTTGAAAGCCACTGGGGCCAATTTGTGGTTAAGAGGTGGTGAGATAAGAAGTGGA
ACGTGACATCTTTGCCAGTTGTCAGAAGAATCCAAGCAGGTATTGGCTTAGTTGTAAGGGCTTTAGGATCA
GGCTGAATATGAGGACAAAGTGGGCCACGTTAGCATCTGCAGAGATCAATCTGGAGGCTTCTGTTTTCTGCA
TTCTGCCACGAGAGCTAGGTCCTTGATCTTTTCTTTAGATTGAAAGTCTGTCTCTGAACACAATTATTTGT
AAAAGTTAGTAGTTCTTTTTTAAATCATTAAGAGGCTTGCTGAAGGAT

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Inflammatory Bowel Disease: Expression of IL-17 Family in Mouse Model of IBD

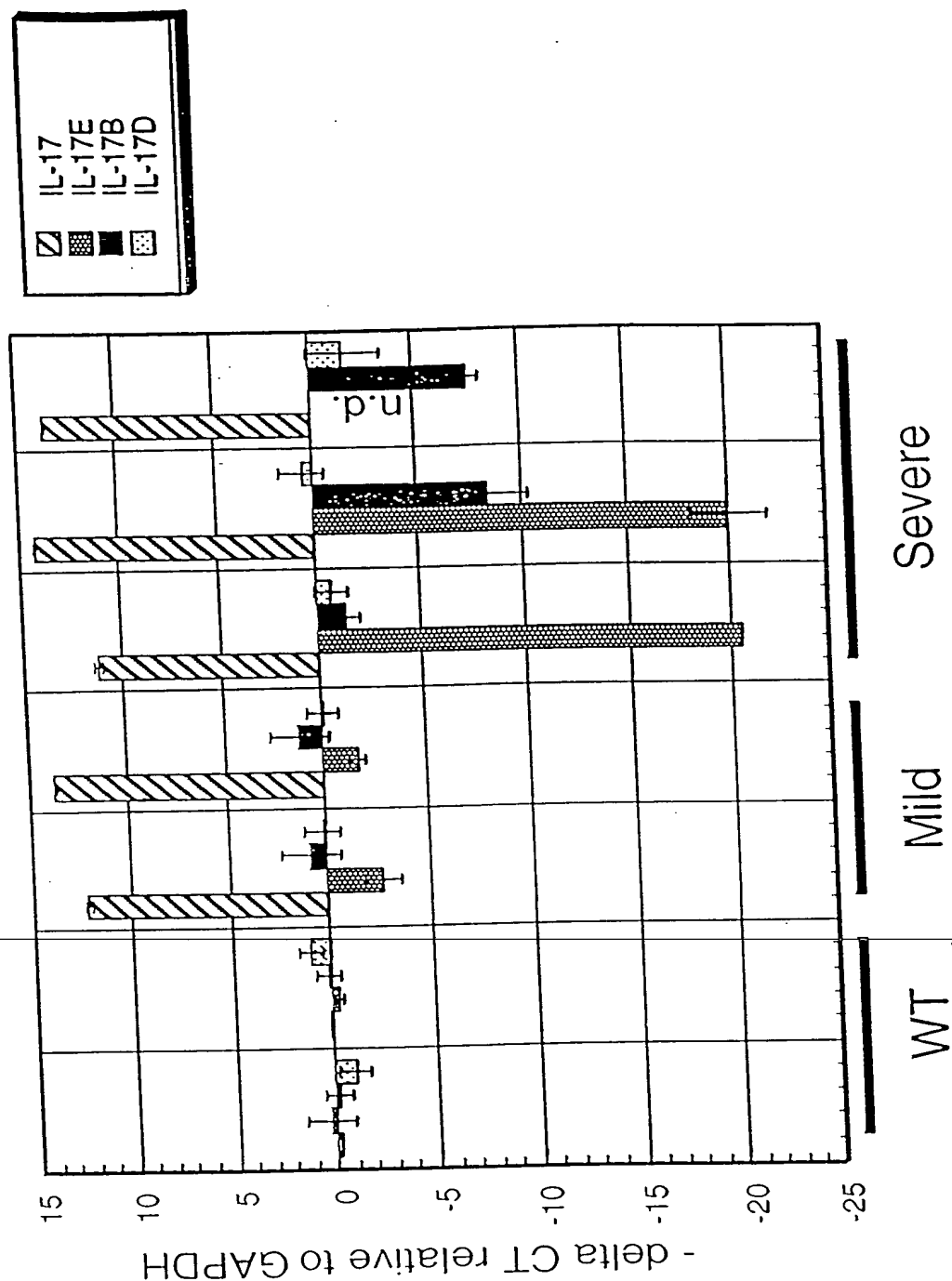


FIGURE 44

IL-17D, present in brain, decreases rapidly following stroke

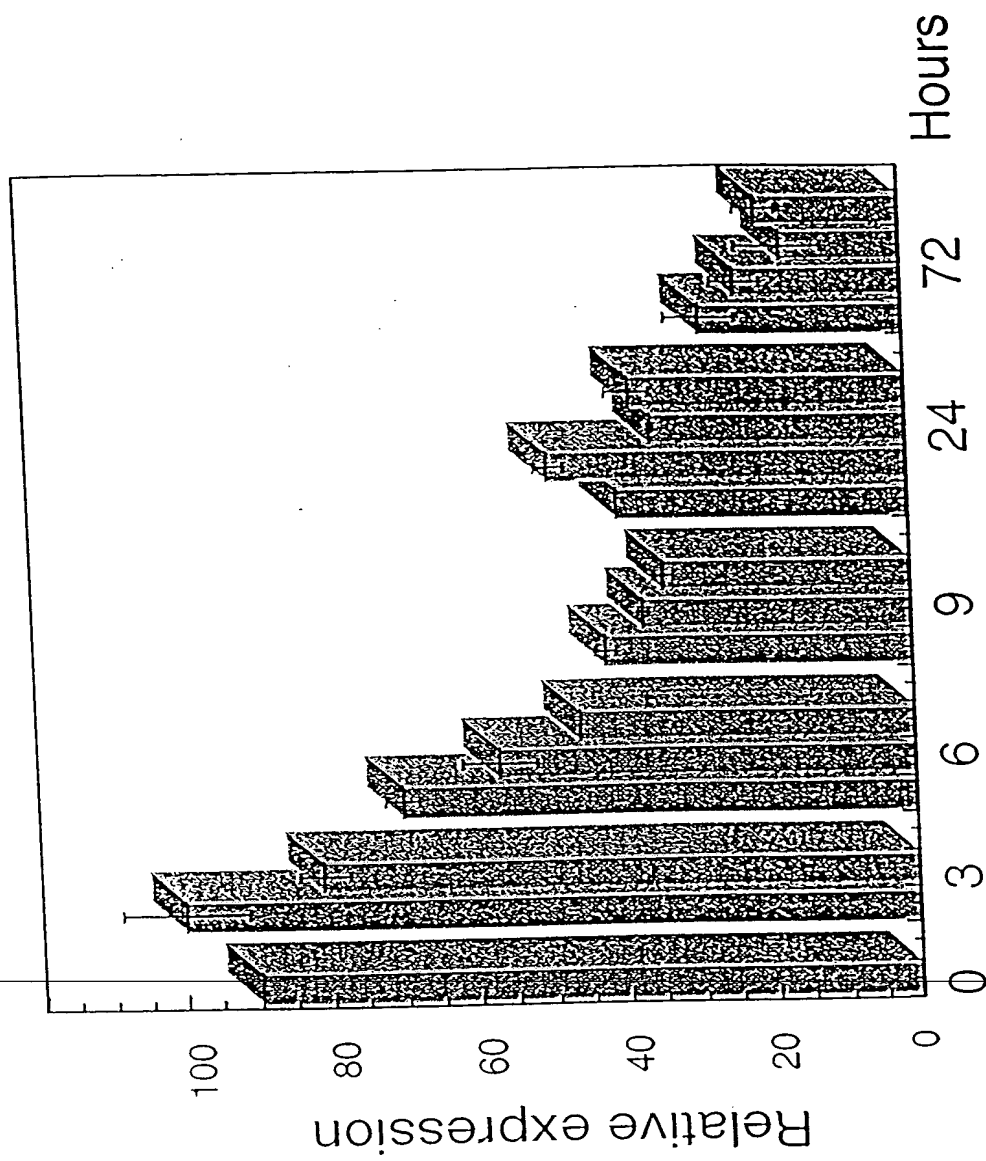


FIGURE 45

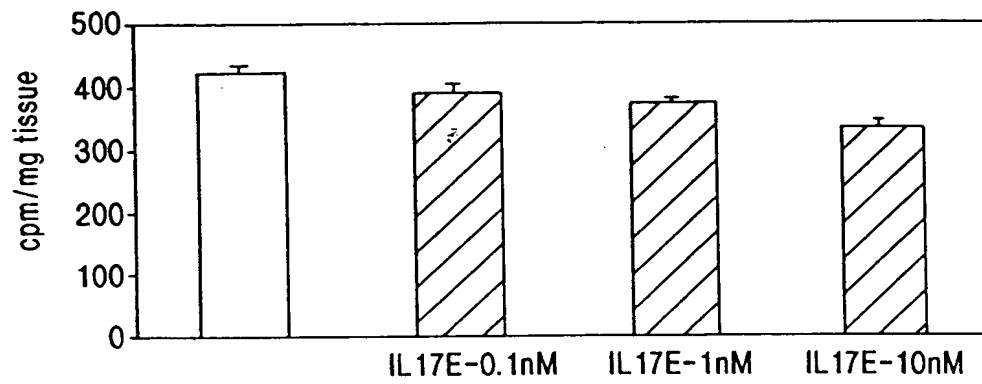
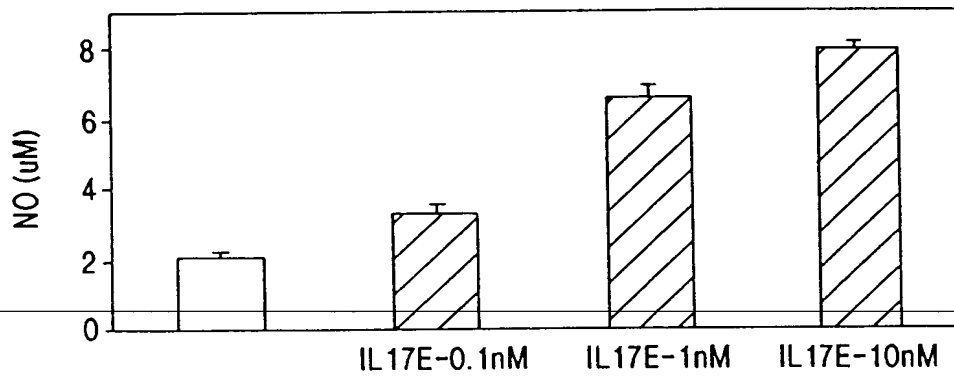
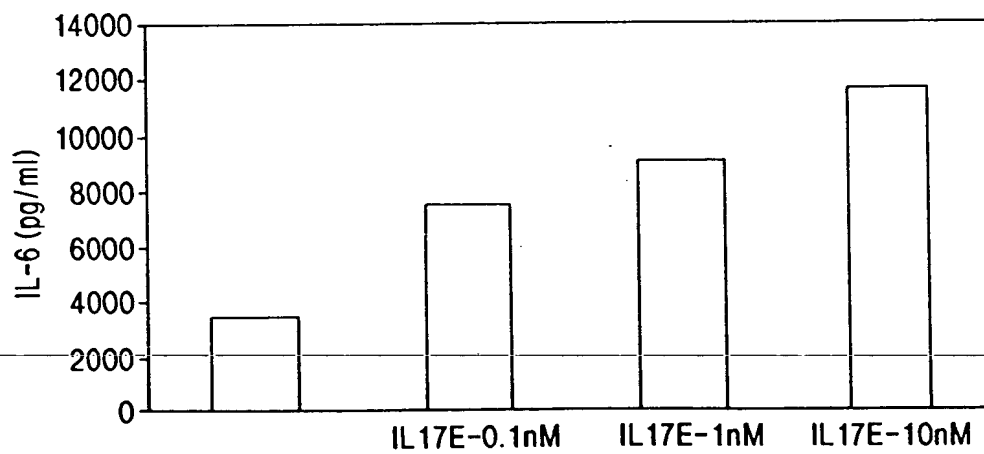
FIGURE 46**FIG. 46A****FIG. 46B****FIG. 46C**

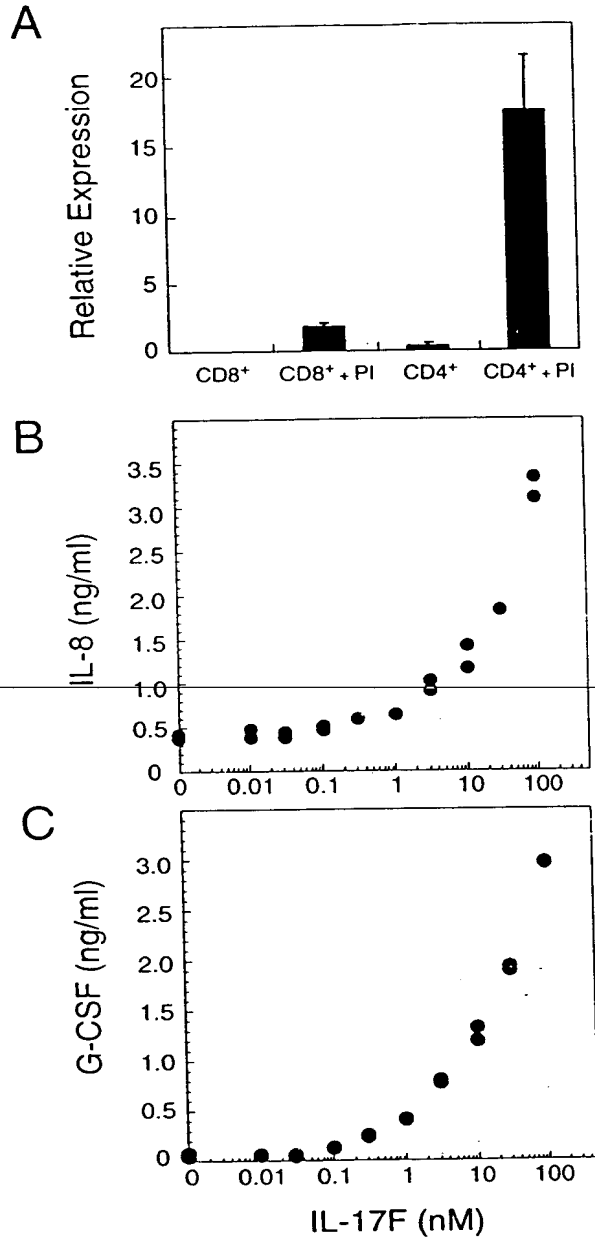
FIGURE 47

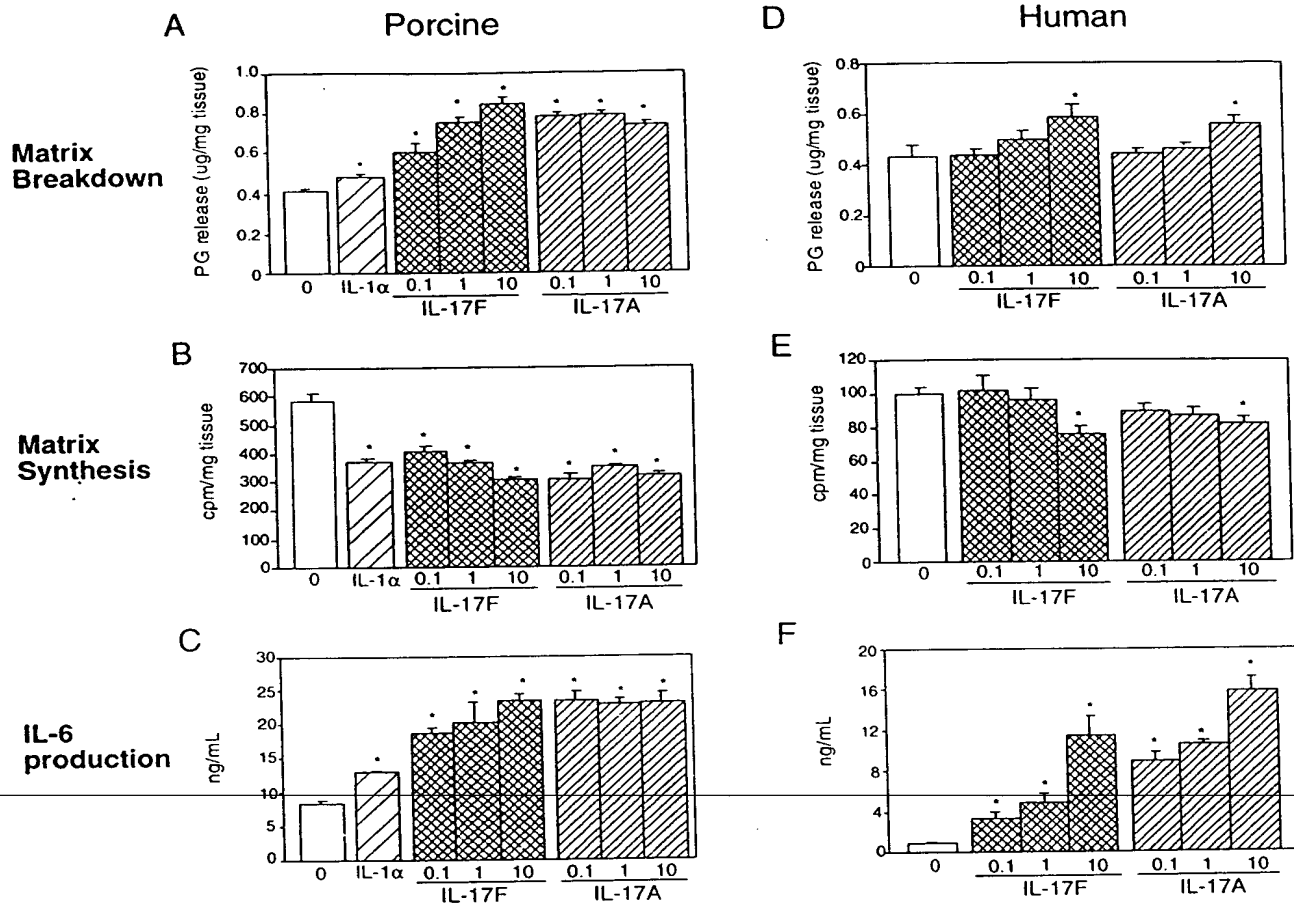
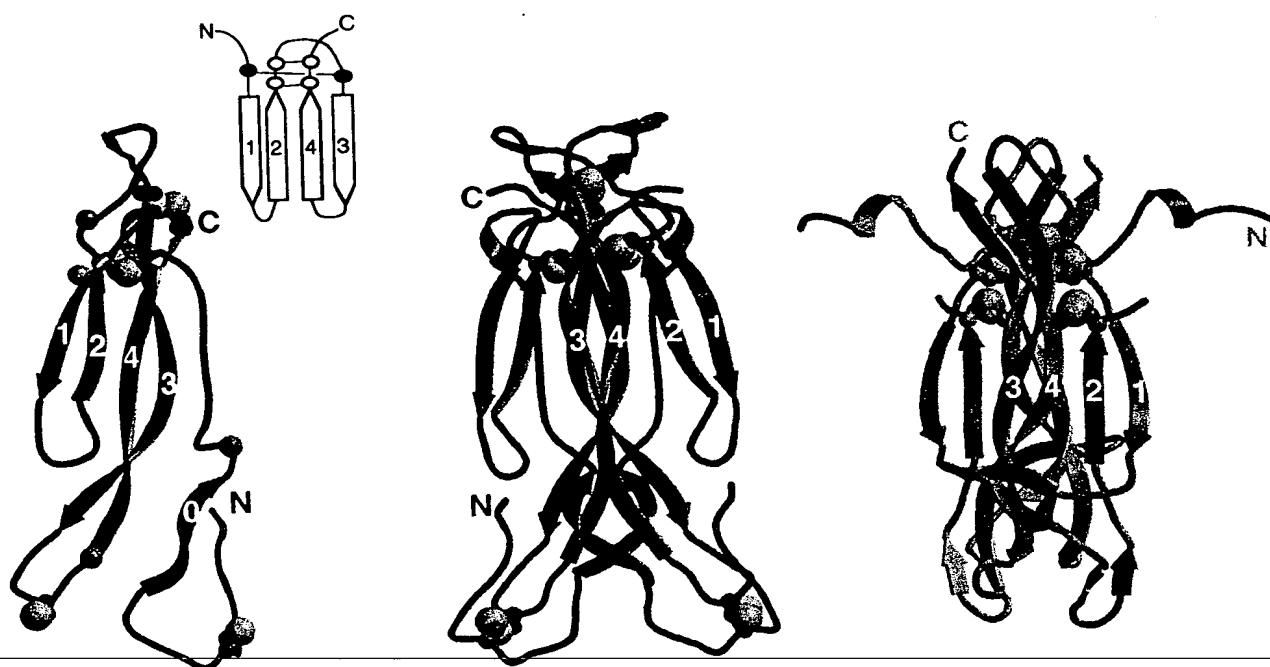
FIGURE 48

FIGURE 49

A

B

C

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FIGURE 50

*

IL-17FRKIPKVG	HTFFQKPES	17
IL-17AIVKAG	ITIPRNP.G	14
IL-17BQPRS	PKSKRKGQGR	PGPLAPGPHQ	VPLDLVSRMK	PYARMEEYER	44
IL-17C	HHDPSLRGHP	HSHGTPHYS	AEELPLGQAP	PHLLARGAKW	GQALPVALVS	50
IL-17EYS	HWPS	QDTSEELLRW	22

0

1

IL-17F	PPVPGG....SMKLDI	GIINENQRV	MSRNIESRST	PWNYTVTWD	59
IL-17A	PNSDKNFPR	TVMVNLNIHN	RNTNTN..PK	RSSDYNNRST	PWNLHRNED	62
IL-17B	NIEEMVAQLR	..NSSELAQR	K-EV....NL	QLWMSNKRSL	PWGYSINHD	88
IL-17C	SLEAASHRGR	..HERPSATT	Q-PVLRPEEV	LEADTHQRSI	PWRYRVDTD	98
IL-17E	STVPVPPLP	..ARPNRHPE	S-RASE....	.DGPLNSRAI	PWRYELDRD	65

2

3

IL-17F	PNRYPSEVVQ	AQ RNLG IN	A..QGKEDIS	MN VPI.QQE	TLVVRKHHQG	106
IL-17A	PERYPSVIWE	AK RHLG IN	A..DGNVDYH	MN VPI.QQE	ILVLRREPPH	109
IL-17B	PSRIPVDLPE	AR L LG VN	PF.TMQEDRS	MV VPV.FSQ	VPVRRR...L	133
IL-17C	EDRYPQKLAF	AE L RG ID	AR.TGRETA	LN VRL.LQS	LLVLR...RP	144
IL-17E	LNRLPQDLYH	AR L PH VS	LQTGSHMDPR	GN ELLYHNQ	TVFYRRP...	112

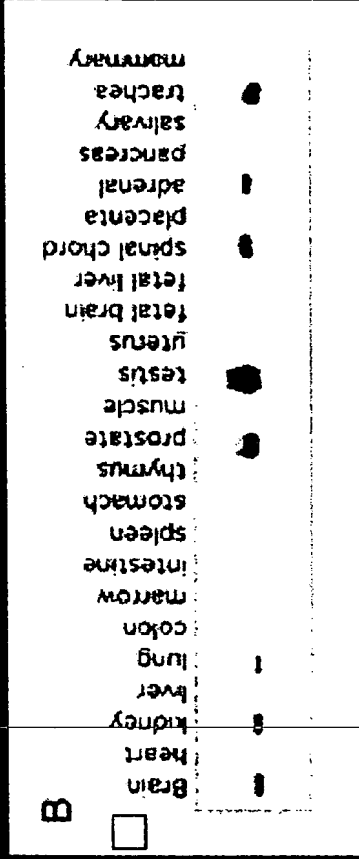
4

*

IL-17F	SV.....SFQLEK	VL..VTVG T	VTPVIHHVQ	...	133
IL-17A	PN.....SFRLEK	IL..VSVG T	VTPIVHHVA	...	136
IL-17B	PPPPRTGP.RQRA	VMETIAVG T	IF.....	...	160
IL-17C	SRDGSGGLPT	PGAFAFHTEF	IH..VPVG T	V.LPRSVAA	ALE	184
IL-17E	HGEKGTHKGY LER	RLYRVSLA V	VRPRVMG..	...	145

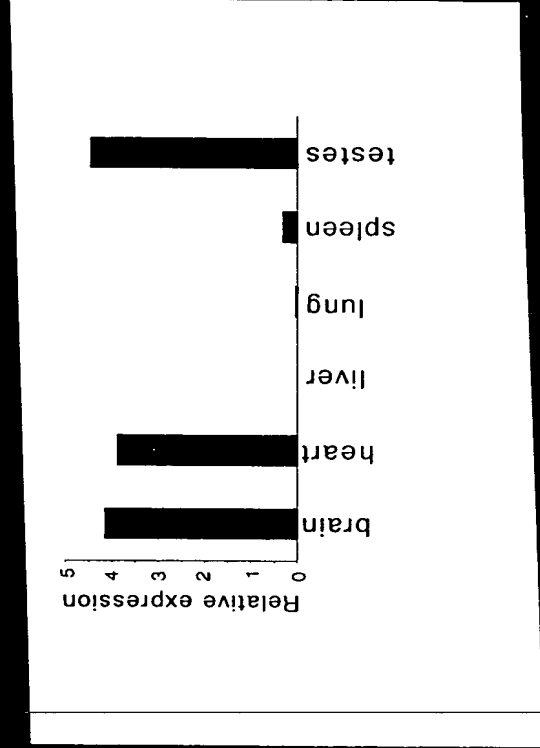
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Tissue distribution of IL-17E



Human

IL-17E (PCR then probed with cDNA)



Mouse

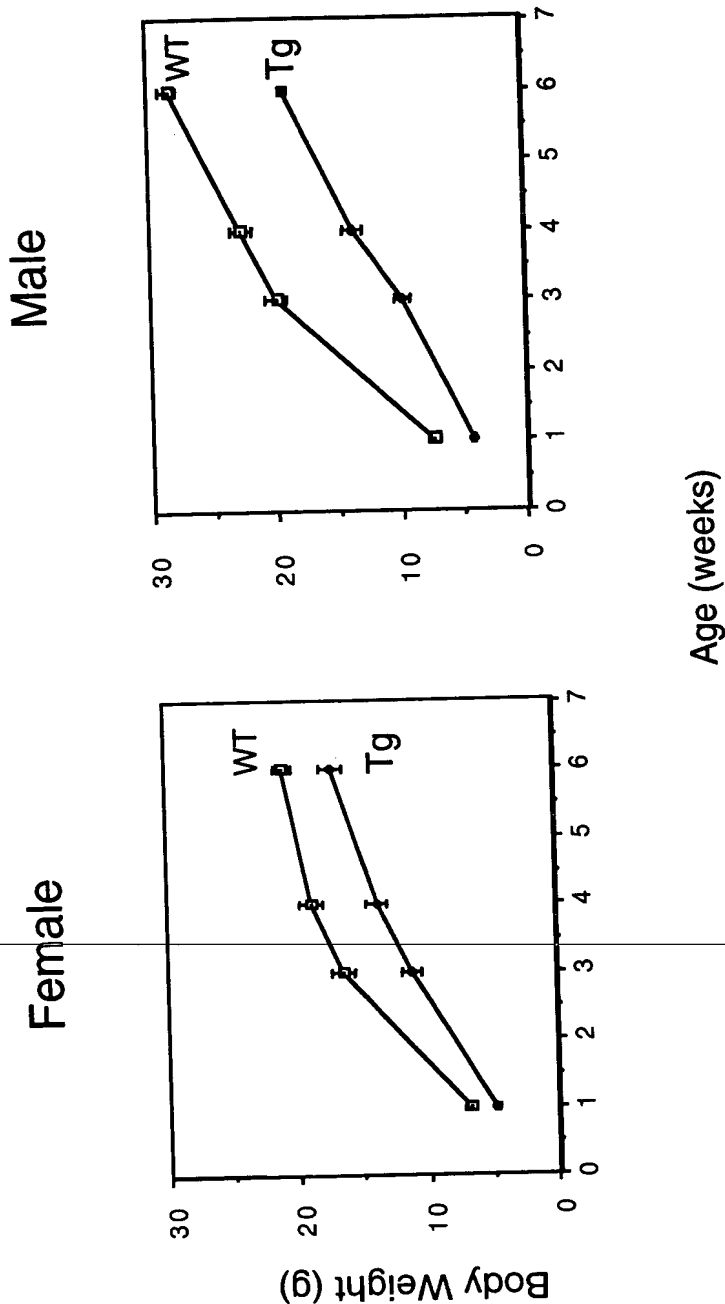
Taqman assay

FIGURE 54

mlL-17E transgenics are growth retarded

FIGURE 55

57/70



IL17E transgenics are jaundiced by 6 weeks of age

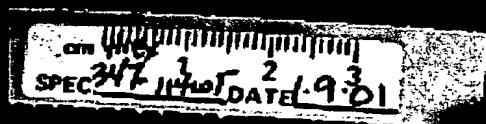


FIGURE 56

FIGURE 57

ml-17E transgenics have elevated
total bilirubin and liver enzymes

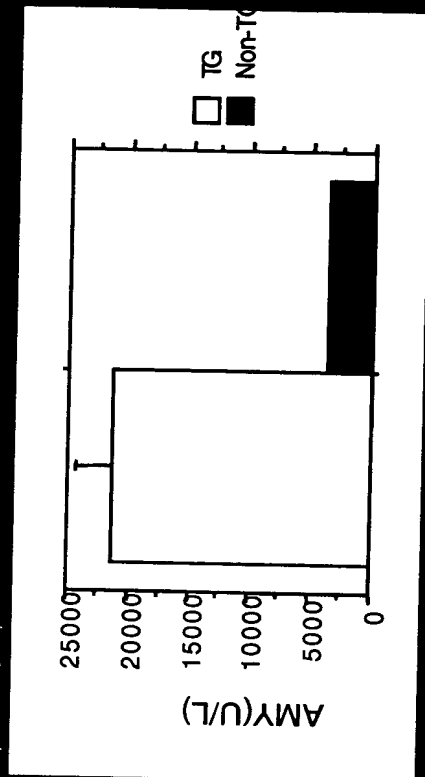
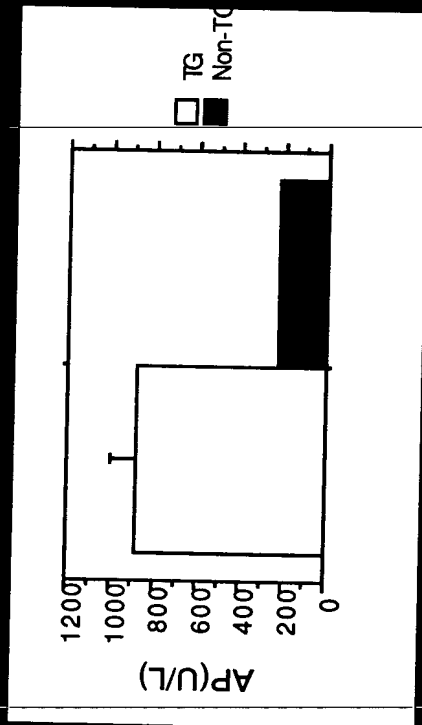
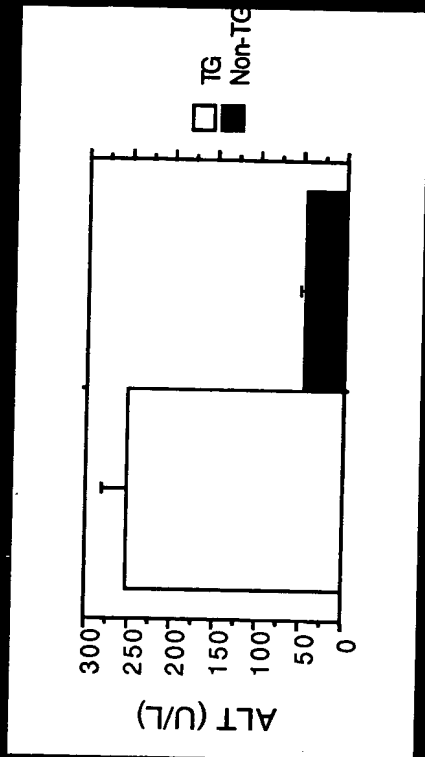
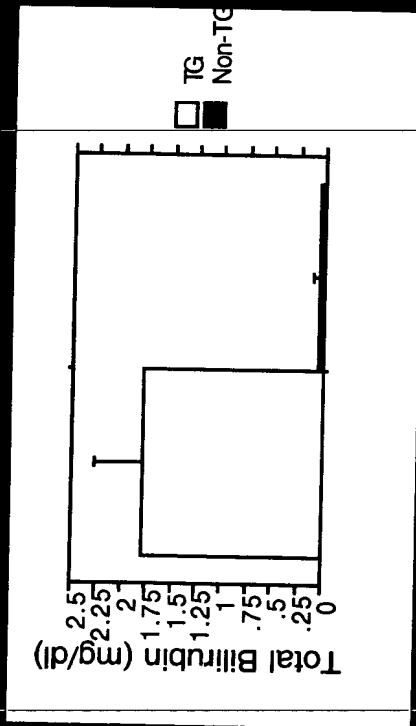
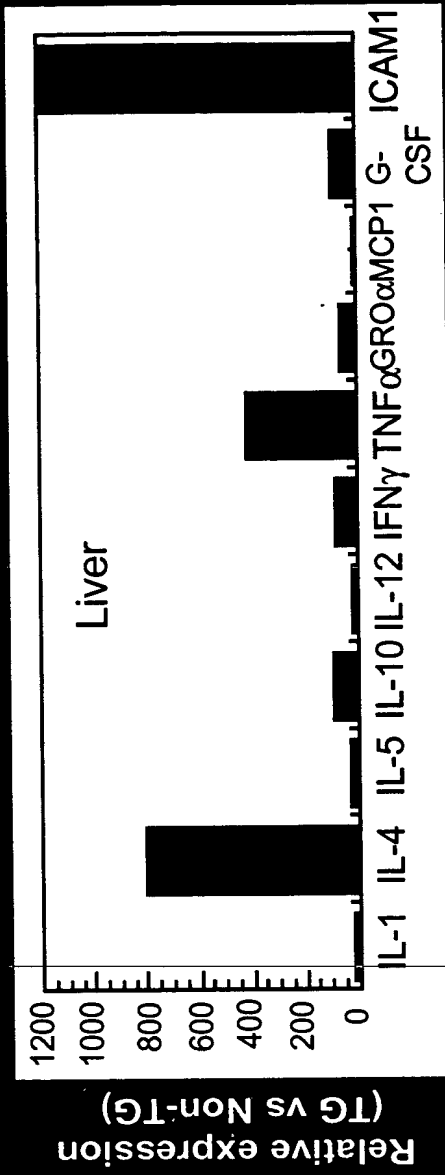
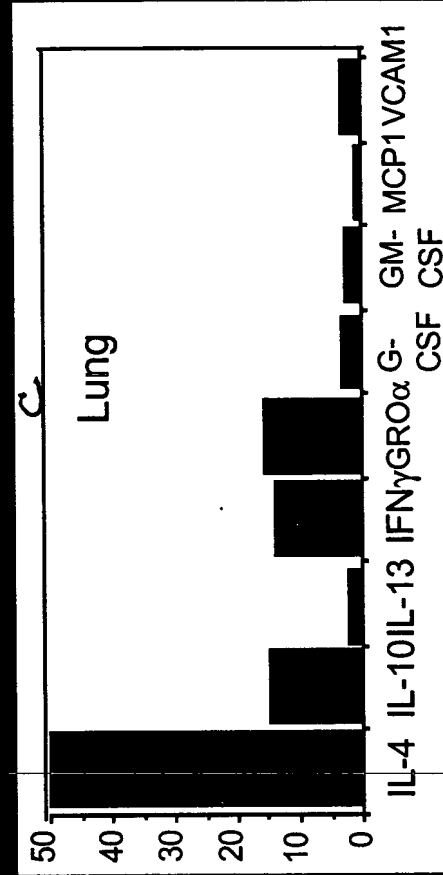
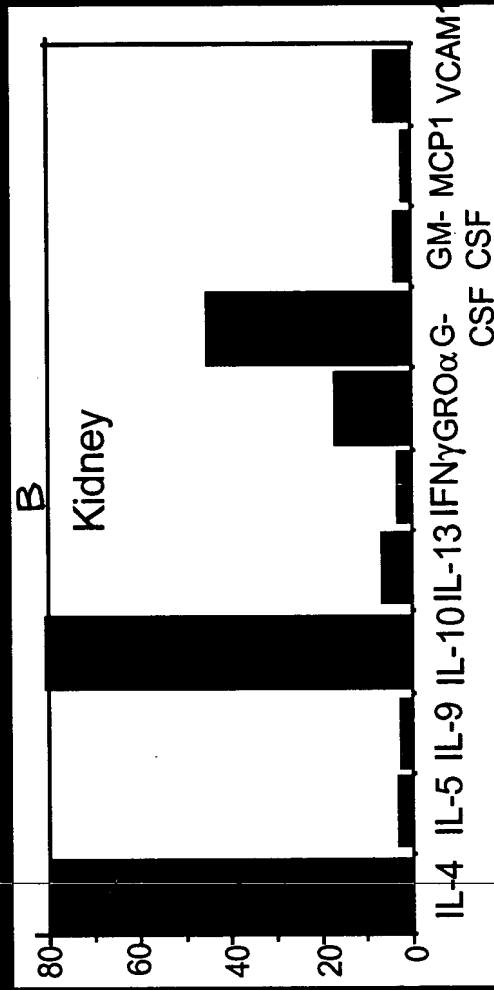


FIGURE 58A



FOOFOOT" /STFOOFOOT

Relative expression
(TG vs Non-TG)



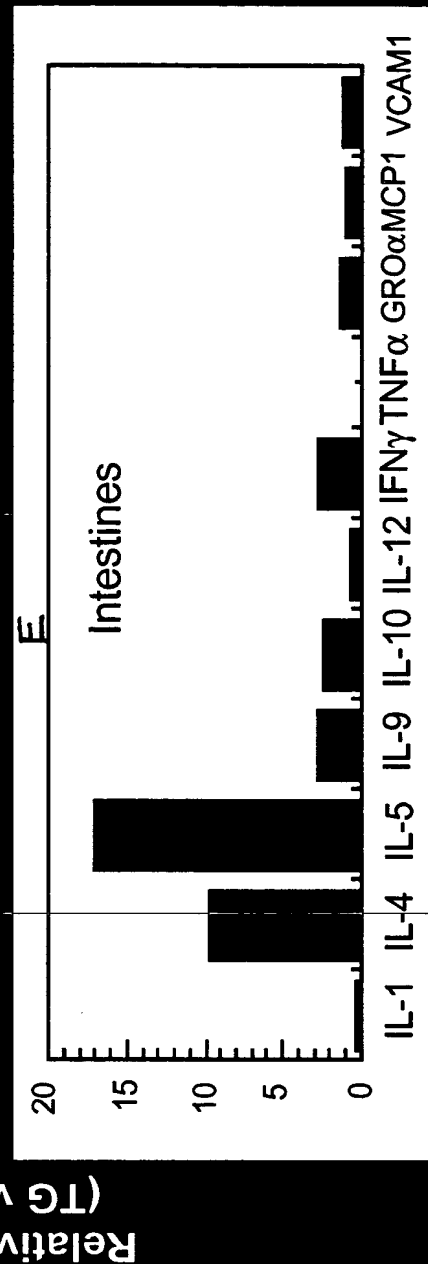
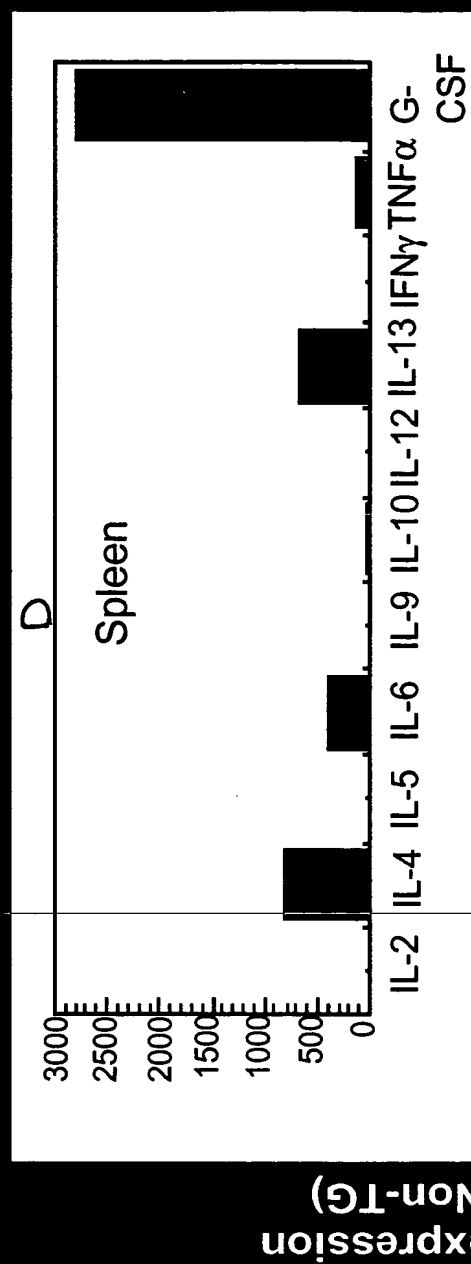


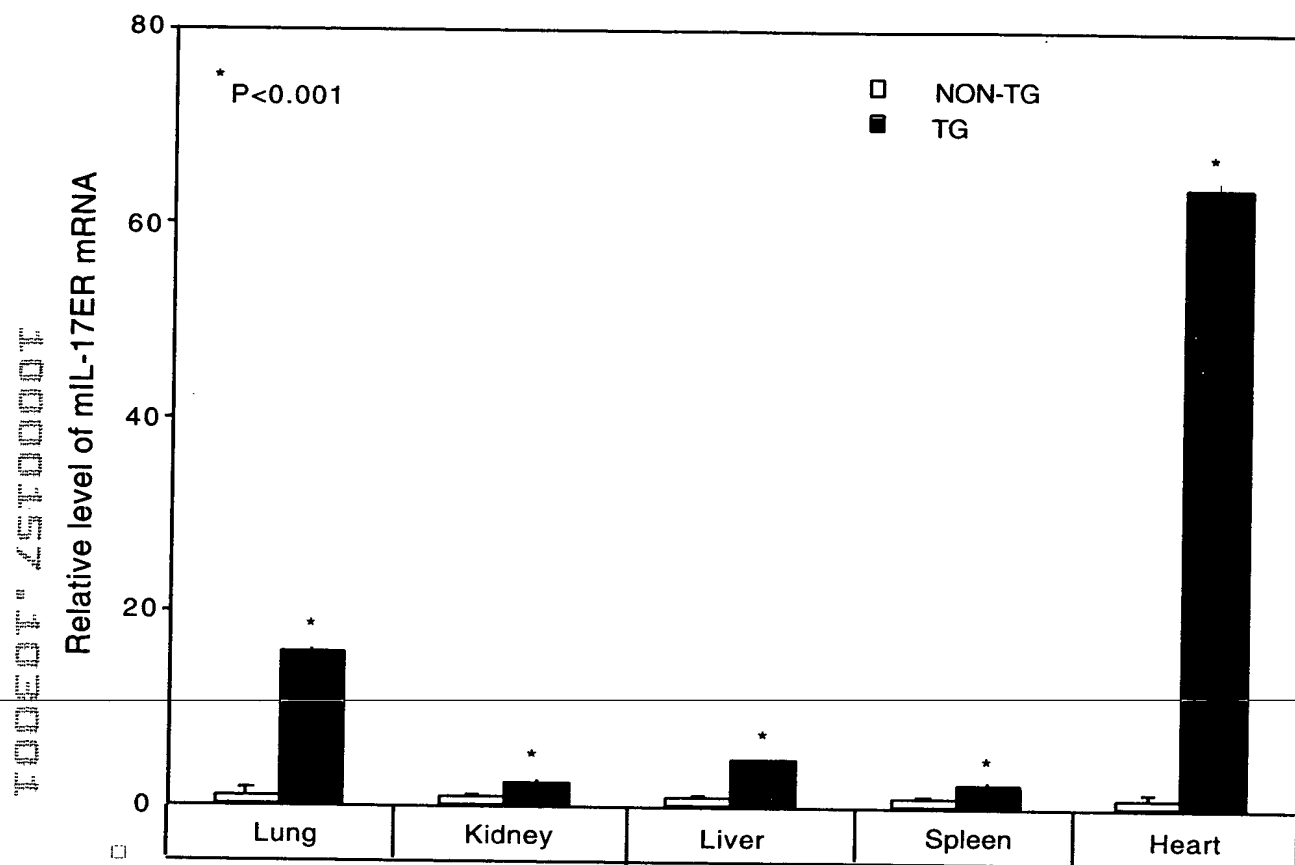
FIGURE 59

FIGURE 60

Elevated serum IL-5, IL-13 and TNF α
in mIL-17E transgenics

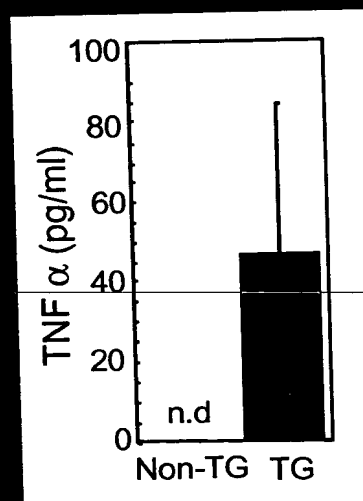
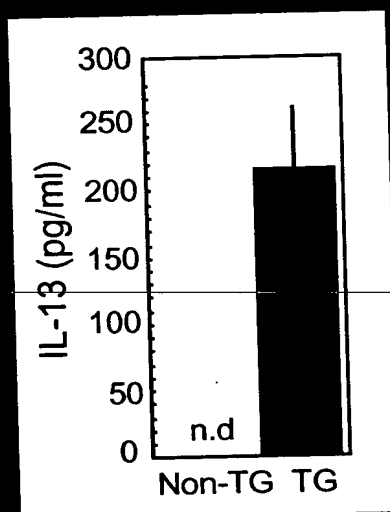
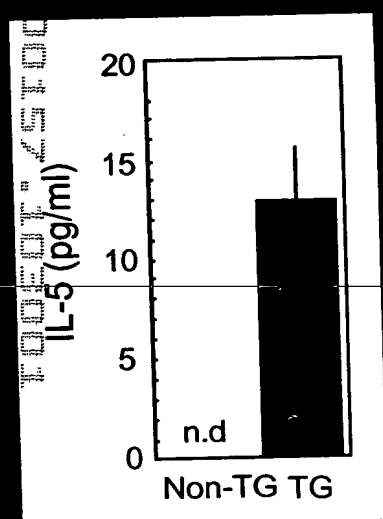


FIGURE 61

Serum IgE and IgG1, but not IgG2a is elevated in mIL-17E transgenics

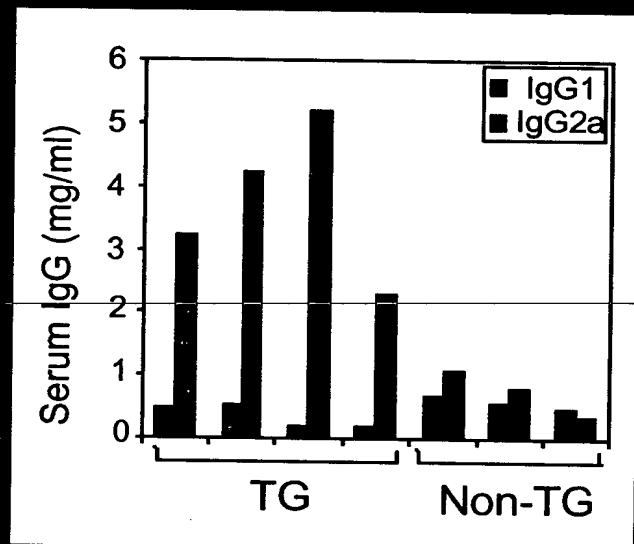
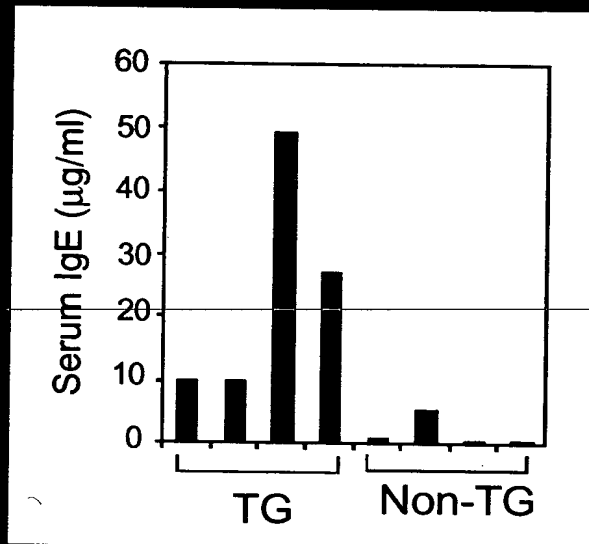


FIGURE 62

Neutrophilia in mIL-17E transgenics (8 wks, PBMC by FACS)

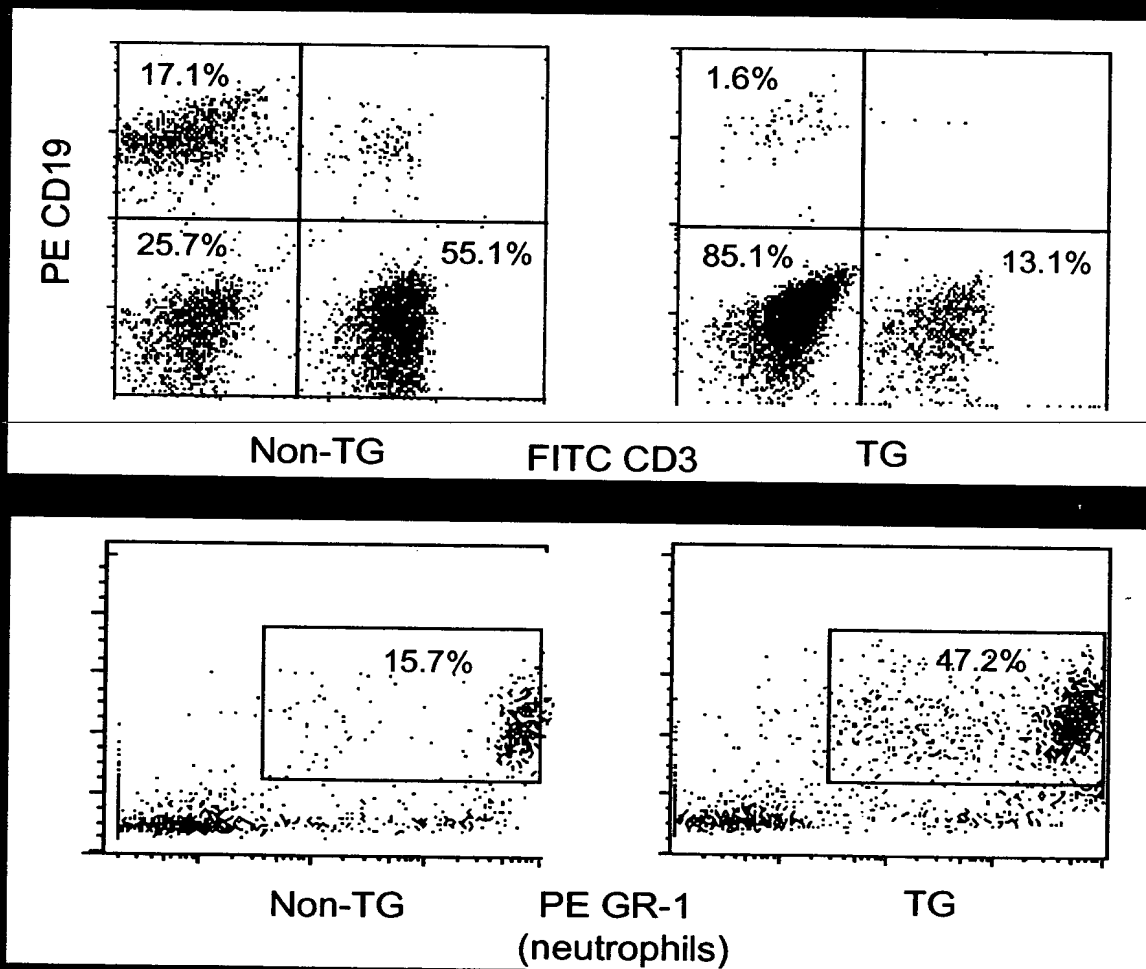


FIGURE 63

Neutrophilia and eosinophilia in mIL-17E transgenics (hematology)

Absolute cell counts ($\times 10^6/\text{ml}$)

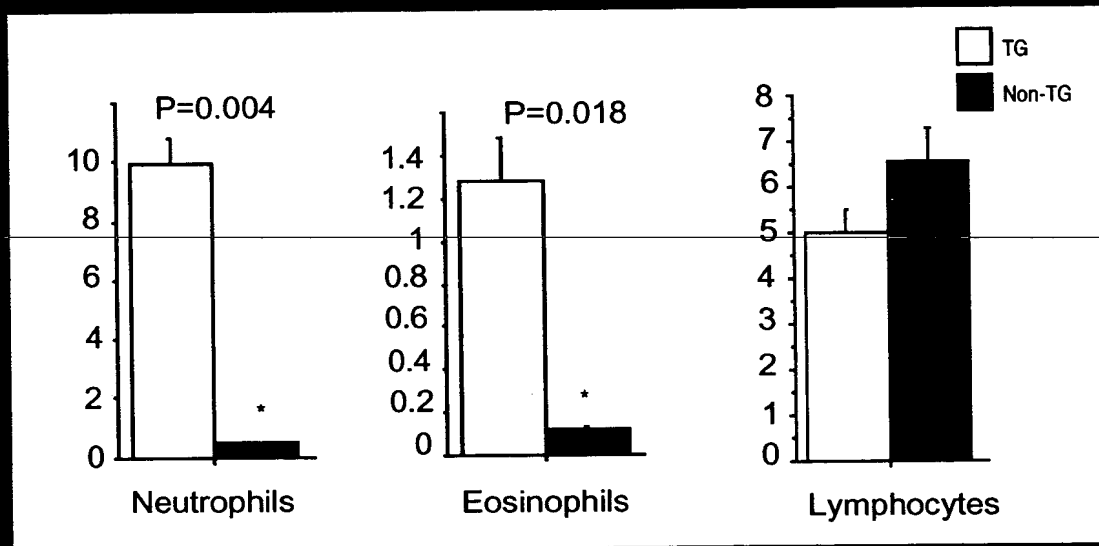


FIGURE 64

G-CSF is elevated
in mIL-17E transgenics

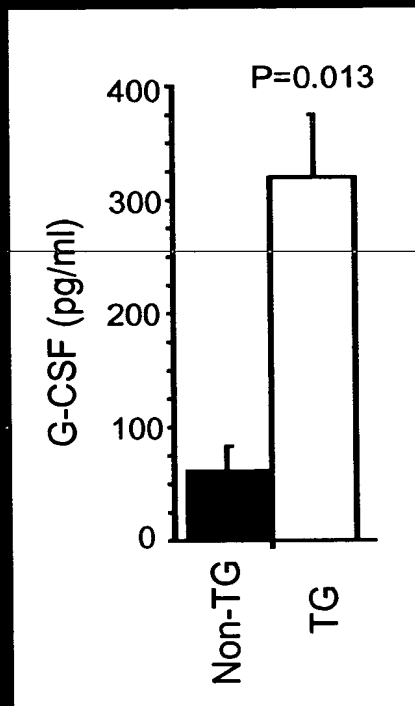


FIGURE 65

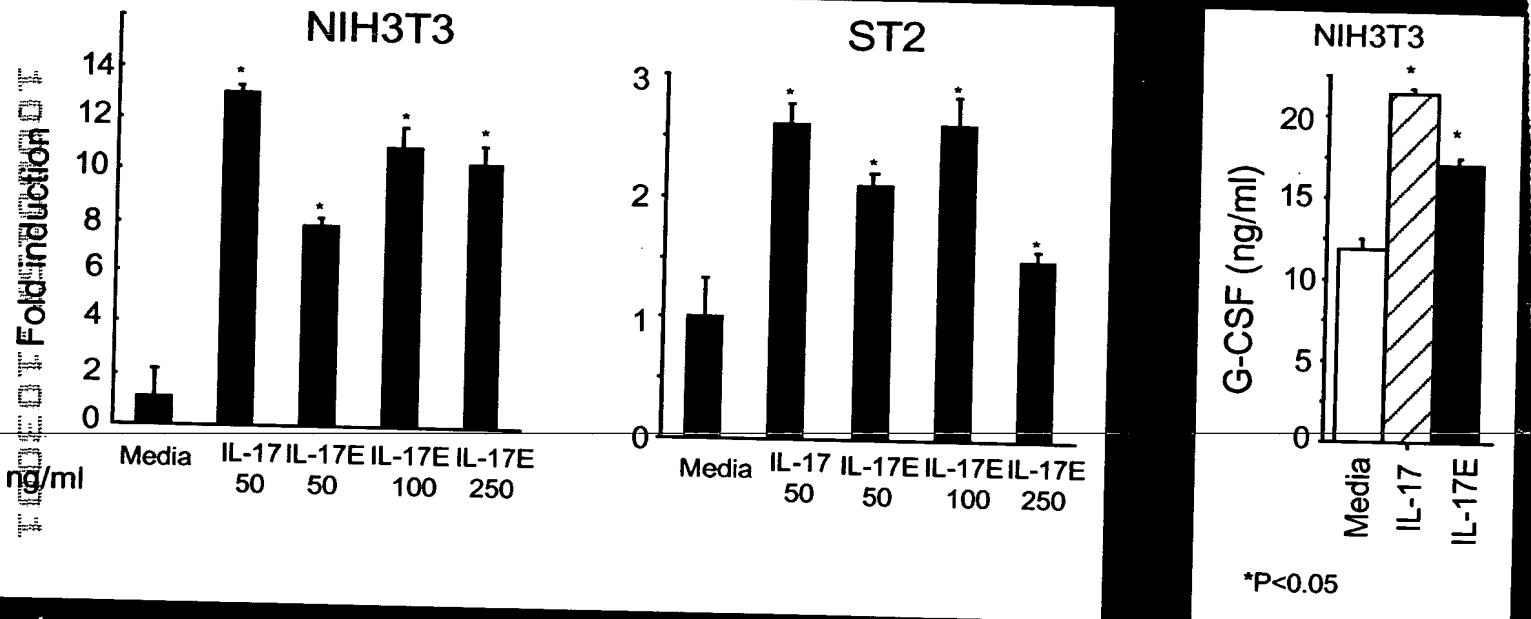
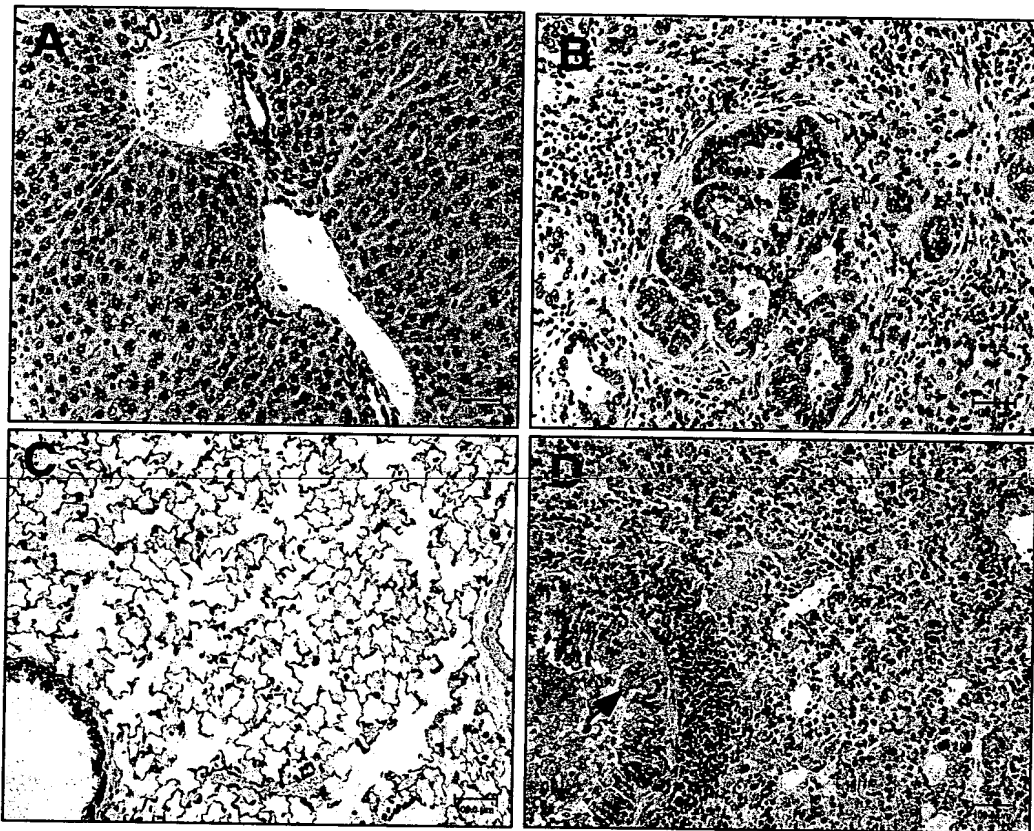


FIGURE 66



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